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Effects of caffeine ingestion and exposure to bright light on alertness, performance, mood, and circadian rhythms (melatonin, temperature) in women during 48 hr of sleep deprivation were tested. In addition, influence of menstrual cycle phase (follicular, luteal) and oral contraceptive use on these measures was assessed. Finally, results of women and those of men (tested previously under similar conditions) were compared. Sleep deprivation decreased alertness/performance and worsened mood but did not affect melatonin and temperature. Caffeine and bright light increased alertness and improved performance as well as reduced melatonin and enhanced temperature. Combining the latter two treatments was the most effective countermeasure to sleepiness. Menstrual phase affected alertness, performance, mood (fatigue), and temperature with higher levels obtained in the luteal group. However, melatonin and temperature were highest in the oral contraceptive group. Circadian rhythms were evident in women across sleep deprivation, treatment group, menstrual phase, and oral contraceptive use. Caffeine delayed melatonin onset while bright light decreased the amplitude and increased the mesor of the temperature rhythm. In general, data of women were similar to those of men. The present investigation suggests that important additional research is needed.

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Pietro Badia 9-12-97

PI - Signature Date

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INTRODUCTION

Subject, Purpose, Scope, and Background

There is compelling evidence from both laboratory and field studies that efficiency is reduced when performance occurs out-of-phase with the normal 24-hr rest/activity cycle (e.g., night work, sustained or continuous operations, rotating shift work). Much of this lowered efficiency is due to the individual's inability to maintain alert wakefulness throughout the work period (Colquhoun, 1984; Krueger, 1989). The latter is especially so under conditions of sustained and continuous operations when work is required during periods normally reserved for sleep. Most of the published research on this topic has focused on the changes observed in men and very little on the changes observed in women.

The present report describes results from a study exploring methods of enhancing alertness and performance in women under sustained wakefulness conditions. Specifically, the effects of caffeine and bright light, alone and in combination, on alertness and performance during 48 hr of sleep deprivation were studied. The effects of these treatments on neurobiological mechanisms underlying changes in alertness and performance, namely melatonin and body temperature, were also explored. The report also addresses factors specific to women, including menstrual cycle phase and oral contraceptive use, which may affect women's responses to sleep deprivation. Gender similarities and differences in psychological and physiological responses to sleep deprivation are discussed. Lastly, the report addresses important theoretical issues that relate to the broader context of circadian rhythms.

In the work setting, nighttime productivity (especially the early morning hours) is reduced both in amount and quality, and accidents and errors are increased (Dinges et al., 1995; Gold et al., 1992; Horne & Reyner, 1995; Lauber & Kayten, 1988). Such problems are believed to be especially acute in certain civilian and military settings where lowered levels of performance, readiness, and errors in judgment can result in accidents of great consequence (Dinges et al.,

1995; Gold et al., 1992; Horne & Reyner, 1995; Lauber & Kayten, 1988). Previous research shows performance efficiency to be related to homeostatic (e.g., Czeisler et al., 1994; Webb & Levy, 1982) and circadian factors (e.g., Akerstedt, 1995; Akerstedt et al., 1979; Badia et al., 1991; Colquhoun, 1984; Czeisler et al., 1994; Folkard, 1990; Krueger, 1989; Smith, 1992).

The homeostatic factor can be operationally defined as the duration of prior wakefulness. In general, as the duration of wakefulness increases, levels of alertness and performance worsen (e.g., Babkoff et al., 1991; Belenky et al., 1994; Czeisler et al., 1994; Dinges & Kribbs, 1991; Horne, 1988; Kleitman, 1923; Patrick & Gilbert, 1896; Webb & Levy, 1982; Wright et al., 1997a). Current theories and research suggest a regulatory role for the neuromodulator adenosine in the homeostatic drive for sleep (e.g., Landolt et al., 1995; Porkka-Heiskanen et al., 1997). Evidence for adenosine's involvement in the homeostatic drive for sleep include: (a) brain adenosine levels increase with increased time awake (Strecker et al., 1997; Haulica et al., 1973), (b) administration of adenosine produces sleep in a variety of mammalian species (e.g., Radulovacki et al., 1989); and (c) neurons in the cerebral cortical neurons (Daly, 1993) and in brain areas which promote wakefulness (e.g., the reticular activating system; Rainnie et al., 1994) are inhibited by adenosine. In addition, the stimulatory effects of caffeine are thought to be due to the antagonism of adenosine receptors in both the central and peripheral nervous systems (e.g., Daly, 1993; Snyder, 1985).

Alertness and performance levels are also regulated by the endogenous circadian pacemaker. Rhythms of the pineal hormone melatonin and of body temperature are thought to reflect the output of the pacemaker located in the suprachiasmatic nuclei of the hypothalamus (e.g., Osborne & Refinetti, 1995; Scott et al., 1995). In general, during the early morning hours (0200 to 0600 hr) when melatonin is high and body temperature is low, alertness and performance are low. On the other hand, during the daytime when melatonin levels are low and body temperature is high, alertness and performance are high (Akerstedt et al., 1979; Czeisler et al., 1994). Melatonin is a hormone thought to have both signaling and hypnotic properties. The hormone is considered the messenger of the circadian pacemaker providing photoperiod information to the organism

(Reiter, 1991a; 1991b; 1991c). Ingestion of the hormone during the daytime or nighttime hours results in decreased alertness, sleepiness, and decrements in performance (e.g., Dawson & Encel, 1993; French et al., 1993; Hughes & Badia, 1997; Lieberman et al., 1984; Waldhauser et al., 1990). Melatonin is also involved in thermoregulation with humans as demonstrated by both correlational and experimental evidence (Badia et al., 1992; Myers et al., 1992). In general, increases in melatonin due to endogenous increases or to exogenous sources results in decreases in temperature. Conversely, decreases in melatonin results in higher temperatures. Such changes are of interest in that the circadian rhythm of body temperature correlates positively with rhythms in alertness and performance. Performance and temperature both rise in the early morning, are high during the day, and trough during the hours when people would normally be sleeping. Regardless of when performance on a particular task is best, performance is almost always at its worst at the temperature trough during the early morning hours (0200-0600 hr).

Research has shown that melatonin secretion and body temperature levels can be controlled and that control of these rhythms results in control of nighttime alertness and performance (Badia et al., 1991; Lewy et al., 1980; McIntyre et al., 1989; Murphy et al., 1995; 1996; Myers & Badia, 1993b, Wright et al., 1997a; 1997b). Specifically, the reduction of melatonin and the enhancement of body temperature results in improved alertness and performance during sustained wakefulness. Two treatments which reduce melatonin, increase temperature and enhance nighttime alertness and performance are caffeine ingestion (Wright et al., 1997a; 1997b) and exposure to bright light (Badia et al., 1991; Campbell & Dawson, 1990; French & Hannon, 1990; Daurat et al., 1993; Dawson & Campbell, 1991; Horne et al., 1991; Myers & Badia, 1993b; Myers et al., 1994; 1995; Murphy et al., 1995; 1996; Wright et al., 1997a; 1997b). Recently our laboratory has shown the combination of bright light and caffeine is more effective in enhancing alertness/performance than either caffeine or bright light alone (Wright et al., 1997b).

Despite the large amount of research conducted on the effects of caffeine and bright light on nighttime alertness and performance during sleep deprivation, no study has considered whether gender differences exist in the response to these factors and to sleep deprivation. There are

several factors specific to women which may influence their ability to maintain alertness and performance during sleep deprivation.

First, hormonal changes due to the menstrual cycle (menstrual, follicular and luteal phase) and the use of oral contraceptives may have differential effects on circadian rhythms of temperature, melatonin, alertness and performance in women. For example, numerous studies show temperature levels change as a function of menstrual cycle phase. Temperature amplitude is lower, and the temperature nadir and mesor are higher during the luteal compared to the follicular phase (Cagnacci et al., 1996; Kattapong et al., 1995; Law, 1986; Lee, 1988; Nakayama et al., 1992; Parry et al., 1997a; Rogacz et al., 1988; Severino et al., 1991; Simpson & Halberg, 1974). In addition, women using oral contraceptives show higher temperature levels compared to normally cycling women (e.g., Lee, 1988; Kattapong et al., 1995). Whether changes in temperature due to menstrual phase and oral contraceptive use affect circadian rhythms in alertness and performance in women during sleep deprivation remains an empirical question.

Research studies on the effects of menstrual cycle phase and oral contraceptives on melatonin levels have yielded conflicting results. Some studies show melatonin levels to be lowest immediately prior to ovulation and highest during the luteal phase of the menstrual cycle (Arendt 1978; 1979; Birau et al., 1981; Brun et al., 1987; Hariharasubramanian et al., 1985; Law, 1986; Potts & Wood, 1972; Webley & Leidenberger, 1986; Wetterberg et al., 1976; Wirz-Justice & Arendt, 1979), while others report that melatonin levels are unaffected by menstrual status (Berga & Yen, 1990; Brzezinski et al., 1988; Cagnacci et al., 1996; Delfs et al., 1994; Fellenburg et al., 1982; Hamilton et al., 1988; Ito et al., 1993; McIntyre & Morse, 1990; Parry et al., 1990; 1997b; Zimmermann et al., 1990). Similarly, some studies show oral contraceptives to increase nocturnal melatonin synthesis (Brun et al., 1987; Webley & Leidenberger, 1986; Webley et al., 1985) while others show that they have no effect (Delfs et al., 1994; Reinberg et al., 1996).

The inconsistent findings with regard to the effects of menstrual phase and oral contraceptives on melatonin levels may be due to methodological differences among studies. First, the sampling frequency of nighttime melatonin levels varies greatly among studies. Second, most of the above studies lacked appropriate experimental control over potential masking agents. That is, none of the studies examined the effects of menstrual phase or of oral contraceptives on melatonin levels using a constant routine procedure. In addition, only one study used a constant routine procedure to examine temperature across the menstrual cycle (Rogacz et al., 1988). The constant routine procedure was developed to control or reduce the influence of masking agents on markers of the endogenous circadian pacemaker (Minors & Waterhouse, 1985; Rietveld et al., 1993; Czeisler et al., 1990). Common masking agents include but are not limited to: ambient illumination, activity, sleep-wake state, food and drug intake, and ambient temperature (Czeisler et al., 1990; Minors & Waterhouse, 1985; Myers & Badia, 1993a; Wright et al., 1997b). The use of the constant routine procedure either eliminates, or distributes uniformly across the circadian cycle environmental and behavioral stimuli which affect measures of the circadian pacemaker, thus allowing a more accurate representation of the endogenous rhythm. Without the level of experimental control afforded by the constant routine procedure and without frequent sampling, spurious findings may result. Thus, a well controlled research study is necessary to elucidate the effects of menstrual cycle phase and oral contraceptives on circadian rhythms in women.

As noted, melatonin and body temperature are thought to be important factors affecting night-time alertness and performance (Badia et al., 1991; Murphy et al., 1991; Wright, 1996). If melatonin and temperature levels vary with changes in a woman's endocrine environment, women may respond differently to sleep deprivation depending upon menstrual cycle phase and oral contraceptive use.

Variation in melatonin and temperature levels due to menstrual phase and oral contraceptive use may also influence the ability of caffeine and bright light treatments to enhance alertness and performance during sustained wakefulness. For example, higher melatonin levels may decrease

the effectiveness of caffeine and bright light treatment, or higher temperature levels may increase the effectiveness of the treatments.

Women may also respond to light differently than men due to psychological (mood) changes associated with the premenses phase. Light therapy with bright light reduces the symptoms of depression, irritability and physical symptoms associated with late luteal phase dysphoric disorder (e.g., Parry et al., 1989). Women's responses to caffeine may also be different than the response seen with men. Specifically, the use of oral contraceptives may affect caffeine's alerting and performance-enhancing properties in women during the nighttime hours. The half life and elimination time of caffeine is considerably increased (increases greater than 200% have been obtained) in women taking oral contraceptives (i.e., caffeine remains in the system for a longer period of time in women using oral contraceptives; e.g., Patwardhan et al., 1980). The effects of this interaction between caffeine and oral contraceptives on alertness and performance during sleep deprivation is unknown.

In addition to investigating the effects of menstrual cycle on various measures during sleep deprivation, this report examines circadian rhythms in women. Circadian rhythms are 24 hour neurobehavioral rhythms important for alertness, the sleep-wake process, immune function, reproduction, and aging (Badia et al., 1992; Dollins et al., 1994; Maestroni, 1993; Myers & Badia, 1995; Reiter, 1991a; 1991b). In humans, there is limited research investigating gender differences in circadian rhythms. Wever (1988) noted that in temporal isolation (an environment free of time cues) the body temperature rhythms of premenopausal women differed from those of both younger and older men whereas the body temperature rhythms of postmenopausal women did not. Specifically, the period was longest in the premenopausal women. Czeisler et al. (1992) noted that older women had a larger circadian amplitude and a higher mean nocturnal temperature than older men. Relatedly, the results of several studies suggest that exogenous estrogen can affect circadian rhythms and sleep (e.g., Wilkinson et al., 1980). Whether mechanisms underlying circadian rhythms derived from data using males are similar to mechanisms derived from data using females is addressed in this report.

In summary, research has shown that nighttime melatonin synthesis and body temperature can be controlled. Control of these rhythms allows enhancement of alertness and performance during sleep deprivation. As noted, ways to achieve this control is by exposure to bright light and by ingestion of caffeine during the nighttime melatonin period.

This report provides data to: (a) evaluate in women the effects of sleep deprivation on various psychological and physiological measures including alertness, performance, mood, and circadian rhythms (melatonin and temperature); (b) assess similarities between sleep-deprived women and sleep-deprived men (tested previously; e.g., Badia et al., 1995); (c) test interventions with women (exposure to bright light, ingestion of caffeine) that are known to be effective with men for increasing alertness and performance during sustained wakefulness; (d) examine the effects of menstrual cycle phase (Follicular vs. Luteal) on women's responses to sleep deprivation (e) examine the effects of oral contraceptives on women's responses to sleep deprivation and on the interventions utilized to increase alertness and performance during sleep deprivation; and, compare these results to women not taking oral contraceptives; (f) determine whether underlying circadian rhythms derived of females are similar to those of males.

Hypotheses

Hypothesis 1--Alertness, Performance, and Melatonin: As noted, melatonin is a hormone with hypnotic properties, and ingestion of melatonin during the daytime or nighttime hours results in decreased alertness, sleepiness, and decrements in performance (e.g., French et al., 1993; Hughes & Badia, 1997; Lieberman et al., 1984; Waldhauser et al., 1990). In addition, reduction of melatonin levels are associated with improved performance (Badia et al., 1991; Wright et al., 1997b). Thus, similar to our earlier results testing male subjects (e.g. Wright et al., 1997a; 1997b), it is hypothesized that suppression of melatonin during the nighttime by exposure to bright light and the ingestion of caffeine will result in increased alertness and performance in

women throughout a 48-hr period of sleep deprivation. Female patterns will be compared with our data with males and similarities and differences noted.

Hypothesis 2--Temperature: As discussed, increases in melatonin due to endogenous or exogenous sources results in decreases in temperature. Conversely, decreases in melatonin results in higher temperatures. Therefore, suppression of melatonin by photic stimulation and the ingestion of caffeine is hypothesized to result in higher temperature throughout a 48-hr period of sleep deprivation. As noted, male and female patterns will be compared.

Hypothesis 3--Oral Contraceptive Use and Caffeine Ingestion: As noted, oral contraceptives increase the half-life and elimination time of caffeine (e.g., Patwardhan et al., 1980). Therefore, it is hypothesized that the ingestion of both substances (oral contraceptives and caffeine) will increase alertness and performance throughout the deprivation period relative to the ingestion of either substance alone.

Empirical Issues

Since both melatonin and temperature levels may change across the menstrual cycle (e.g., Rogacz et al., 1988; Webley & Leidenberger, 1986), no hypothesis concerning alertness and performance during the two phases is offered because a case for competing hypotheses can be made (i.e., in the Luteal phase, higher melatonin could result in worse performance and higher temperature could result in better performance). Therefore, this important question remains to be tested empirically.

Similarly, oral contraceptive use may increase both melatonin and temperature levels (e.g., Arendt, 1978; 1979; Potts & Wood, 1972; Webley & Leidenberger, 1986), no hypothesis concerning alertness and performance in women using these drugs relative to those not using them is offered because competing hypotheses are equally tenable.

BODY

Experimental Methods, Assumptions, and Procedures

Subjects

Ninety-seven healthy, female participants (aged 18-28 years) who gave written informed consent participated. Subjects showed regular sleep-wake schedules (self reported bedtime between 2300 and 0200 hr and wake-time between 0700 and 1000 hr) and were low to moderate habitual caffeine users < 250 mg day. Only low to moderate caffeine users were tested to minimize tolerance and withdrawal effects. Sleep schedules and caffeine intake were verified with logs for the week prior to study. In addition, subjects were free from nicotine and medication use (except oral contraceptives). Alcohol and caffeine use was prohibited for 24 hr prior to participation. Because of their effects on melatonin levels, nonsteroidal anti-inflammatory drugs were prohibited for 72 hr (Murphy et al., 1996). Participants reported consistent regular menstrual cycles of 25-32 days in length for 6 months and were required to keep menstrual cycle logs for at least 1 month prior to participating. Women using oral contraceptives reported continuous use of a combination oral contraceptive for at least 2 months prior to participation (The earliest a participant was tested was during the third month of contraceptive use. The Appendix provides background information on each subject including the type of contraception used. All participants obtained a physical exam at the Student Health Center as well as a pregnancy and progesterone test 1 day prior to participating in the study. The pregnancy test was used as a precautionary measure to ensure the health of the woman and fetus. No pregnant women were tested. Progesterone levels were recorded to ensure the luteal phase of their menstrual cycle. Progesterone was assessed using serum samples. A single sample of blood (1 ml) was drawn at the University Health Center by a Registered Nurse after a 12 hr fast. This sample was collected during the morning hours (0800-1000 hr) the Wednesday prior to participation on Thursday. The blood sample was assessed for progesterone content by radioimmunoassay (Roche Biomedical Laboratories, Dublin, OH). Participants were tested in either the Follicular, Luteal and in the

pseudo-luteal phase for those using oral contraceptives. Blood sampling occurred on cycle Day 9 ± 2 after menses for women in the Follicular phase and on cycle day 20 ± 3 after menses for women in the Luteal phase. Progesterone levels exceeding 4.1 mIU/ml are representative of the luteal phase. Five of the 35 women tested in the Luteal Phase according to Menstrual Logs showed low progesterone levels consistent with the Follicular phase.

Over 1,500 subjects were screened (see Reasons People were Excluded from Participation section of Appendix for additional details). Of the 97 subjects tested, data for at least 1 night of sleep deprivation is available for 75 individuals. A total of 59 subjects completed both nights of the study. A number of difficulties occurred when trying to schedule subjects for participation (see Difficulties Scheduling Subjects section in the Appendix for additional details) First, our rejection rate for the current study is around 85% whereas in previous studies testing males (e.g., Badia et al., 1995) rejection rates were lower (on average 75%). In addition, of those meeting the screening criteria in previous work, 92% have participated whereas in the current study, only 33% of individuals qualifying for the study have participated. The latter percentage was expected given our interest in menstrual cycle phase and oral contraceptive use. Reasons for losing participants are described in detail in the Appendix.

The average age and weight of participants were 20 years and 60 kg (133 lb), respectively. Subjects' age and morning-eveningness type (Horne & Osterberg, 1976) were similar for each treatment condition. However, the average weight was not similar across groups (see Background Information section of Appendix for the average weight in each condition). Subjects were paid $150 for their participation.

Groups

There are nine experimental conditions (Table 1) addressing the hypotheses concerning exposure to bright light, caffeine ingestion, oral contraceptive use, and appropriate control groups. With the exceptions of menstrual cycle phase and oral contraceptive use, participants were randomly assigned to one of four conditions (Dim Light-Placebo, Dim Light-Caffeine, Bright Light-Placebo, Bright Light-Caffeine).

Table 1. Subjects and conditions tested.

	Follicular Phase	Luteal Phase	Oral Contraceptive
Dim Light-Placebo	n = 8	n = 11	n = 8
Bright Light-Placebo	----	n = 8	n = 8
Dim Light-Caffeine	----	n = 8	n = 8
Bright Light-Caffeine	----	n = 8	n = 8

Notes. ---- = condition not tested.

Protocols

Laboratory testing began at 1930 hr Thursday and continued until 1000 hr Sunday. Participants slept from 2400 to 1000 hr Thursday evening. After awakening, they remained awake for the next 48 hr. A modified constant routine procedure was used (Czeisler et al., 1990; Minors & Waterhouse, 1985; Wright et al., 1997a). During the daytime (0800 to 2000 hr), ambient illumination was maintained at ≤ 88 lux. One subject was assigned to each experimental room where they remained seated (nonrecumbent) in chairs throughout most of the study. Ambient temperature in the rooms was maintained at 24 ± 2 °C (76 ± 3 °F). Food was provided in aliquots every 3 hr. The diet was based on 3,000 cal/day (RDA + 40%; USDA, 1981) to allow for increased energy need during sleep deprivation. Each aliquot consisted of approximately

375 cal. From 2000 to 0800 hr, subjects remained under either dim (< 88 lux) or bright (> 5,000 lux) illumination depending on the treatment condition. Light sources in the "bright light room" consisted of a bank of three light boxes; from Lighting Resources (Columbus, OH, USA) and Apollo Light Systems (Orem, UT, USA), placed approximately 1 m in front of the subjects. In addition, one 500 watt halogen lamp, shielded from direct illumination of the eyes, illuminated the background. During performance testing on computers, light intensity was reduced to a minimum of 2,000 lux to reduce glare on the computer screens. In addition, subjects wore black-colored hospital outfits ("scrubs") and an antiglare shield was placed on the computer monitor to prevent light glare from interfering with performance testing. At all other times from 2000 to 0800 hr, subjects received approximately 5,000 lux (approximately 2 hr of each 3 hr testing block). All lux measurements were taken at eye level. Half the subjects in each lighting condition received either placebo (200 mg sugar) or caffeine ("Eleveine—Alva-Amco Pharmaceutical Co., Chicago, IL, USA) in doses of 100 mg four times a night or 200 mg two times a night. For the first 15 subjects tested, either caffeine or a placebo was administered in a double-blind manner with water and food at 2000 and 0200 hr each night. The caffeine protocol was modified following reports by several subjects that they experienced stomach upset and nervousness. All subsequent subjects were given 100 mg of caffeine 4 times a night (2000 hr, 2300 hr, 0200 hr, 0500 hr) instead of 200 mg twice each night (2000 hr and 0200 hr). The total amount of caffeine ingested each night remained at 400 mg.

When subjects were not performing tasks, they were permitted to watch taped movies, play video games (1000 to 1800 hr only), read, do homework, play cards or converse with a member of the research staff. A member of the staff remained with the subjects at all times except during collection of EEG data.

Measures

Several neurobehavioral measures were used to examine alertness and performance during the nighttime hours. These measures were recorded in 3 hr blocks from 2000 to 0800 hr each night.

Performance batteries were composed of tasks from the Walter Reed Performance Assessment Battery, the United Tri-service Performance Assessment Battery, and several tasks from the sleep laboratories of the University of Pennsylvania and Bowling Green State University (Dinges et al., 1993; 1994; Gillooly et al., 1990; Thorne, 1990; Thorne et al., 1985). Performance tasks included are listed in Table 2 and detailed descriptions for each task are provided in the Performance Battery section of the Appendix.

Table 2. Types of tasks administered.

Cognitive Performance

Short Term Memory / Working Memory Tasks

- Switching Task - Math Throughput (divided attention)
- Two Column Addition
- Digit Recall
- Reaction Time Task - Time Uncertainty Block
- Dual Task-Throughput (divided attention)
- Continuous Recognition

Long Term Memory Tasks

- Probed Force Memory Recall 6 - word pair version

Spatial Processing / Coordination Tasks

- Dual Task - Control Losses (divided attention)
- Switching Task - Mannequin Throughput (divided attention)

Reaction-Time-Based Performance Tasks

- Modified Psychomotor Vigilance Task
- Wilkinson Four Choice Reaction Time

Subjects practiced performance tasks from 2000 to 2400 hr Thursday night as well as from 1100 to 1800 hr Friday day. Each subject practiced tests until asymptotic performance was obtained (i.e., less than a 10% change in performance between the last two practice trials).

Only throughput scores were analyzed except for tasks not having a throughput score. Throughput is derived from accuracy and speed data yielding a measure of correct responses per minute. The throughput measure is thus sensitive to changes in accuracy and speed performance.

Measures of alertness included the Maintenance of Wakefulness Test (MWT; Mitler et al., 1982), Stanford Sleepiness Scale (SSS; Hoddes et al., 1973), Profile of Mood States (POMS; McNair et al., 1981) and spectral analysis of the EEG (see Alertness Assessment section of Appendix for additional details). These measures were recorded during each 3-hr block across the successive 24-hr periods. Latencies to sleep on the MWT were scored using the criteria of Rectschaffen and Kales (1968). Sleep onset was defined as the first epoch of stage 2 sleep. If participants remained awake for 15 min on the MWT, the test was ended and a score of 15 was given for that test. For MWT and spectral data, EEG activity was acquired over 3 brain sites (Fz, Cz, Oz) referenced to linked mastoids using a Grass Model 7 Polygraph. Standard mentalis EMG, and EOG activities were also recorded to assist in sleep stage scoring. Each EEG amplifier (Grass model 7P511) was set at a sensitivity of 5 μv/mm and used a frequency bandwidth (filter settings) of 0.3 to 100.0 Hz. A 60 Hz notch filter was used to attenuate electrical interference noise. A 50 μV sign wave signal was used for calibration. Impedances for the EEG electrodes were maintained at less than 10 kΩ. For EEG spectrals, 1 min of eyes closed data were acquired at a rate of 256 samples per second per channel with a 12 bit Data Translations 2821 A-to-D board. Data were assessed for changes in amplitude by submitting the digitized EEG data to a Fast Fourier Transform (FFT) in manually selected epochs (Rhythm v. 9.0; Stellate Systems, Westmount, Canada). The EEG data were then accumulated in power ($\mu V^2/Hz$) over a frequency bandwidth of 1.5 - 30.0 Hz, in 1s bins for each minute. Artifacts were removed from data prior to analysis. Spectra of epochs with EEG artifacts (e.g., muscle artifact, amplifier blocking) were eliminated on the basis of visual inspection. If fewer than 30s of artifact free epochs were

available, the spectral was omitted from further processing. The Profile of Mood States (POMS; McNair et al., 1981) and the Positive Affective Negative Affective Scale (PANAS; Watson et al., 1988) were also administered in each three hour block to measure mood across the deprivation period.

Melatonin content in saliva was measured on both nights of sleep deprivation. Approximately 2 ml of saliva were collected (unstimulated) into polystyrene tubes every 1 hr from 2000-1000 hr. Saliva was always gathered prior to administration of food and subjects were required to brush their teeth (without toothpaste) and rinse their mouths after every food aliquot. All samples were immediately centrifuged at 2,500 rpm for 5 min and frozen at -20 °C until assayed. Saliva melatonin levels were determined by radioimmunoassay I^{125} (Alpco, LTD., Windham, NH, USA) performed by the Radioimmunoassay Laboratory of Fort Rucker (Fort Rucker, AL, USA). Briefly, this commercially available assay uses extraction procedure and melatonin content was measured in duplicate. The minimum level of detection (defined as the concentration at 2 SD from the counts at maximum or zero binding) was 0.3 pg/ml. The interassay coefficients of variation for low and high controls were 11.03 and 9.86 respectively and the average intra-assay coefficient of variation was 9.59%. Results for 5 saliva samples were suspect as the amount of melatonin measured did not correspond with the results for samples immediately prior to or after. That is, melatonin levels of 3 ± SD from the adjacent samples were observed. These questionable samples were replaced with an average of the sample prior to and the sample immediately after.

Tympanic temperature ("First Temp", Intelligent Medical Systems, Carlsbad, CA, USA) was recorded every half hour during the evening and every hour during the daytime. A minimum of two measures that differed by no more than 0.056 °C (0.1 °F) was required for reliability at each measurement. If the two measurements were not exactly the same, the higher of the two was used.

Analyses

Data for melatonin, temperature, mood, and alertness and for performance measures listed in Table 2 were analyzed using repeated measure ANOVAs. Melatonin and temperature data as repeated factors were analyzed hourly from 2100 to 0800 hr each night and alertness and performance data were analyzed across 4 test blocks per night. A morning assessment of alertness on the MWT was also performed. Each performance task has multiple measures that can be examined (see Performance Battery section of Appendix). Only throughput scores were analyzed except for tasks not having a throughput score. Throughput is derived from accuracy and speed data yielding a measure of correct responses per minute. The throughput score is thus sensitive to changes in accuracy and speed performance.

In addition to the examination of nighttime temperature levels, circadian temperature values for individual subjects were computed using data from 1100 to 1000 hr each day and tested for treatment differences (Brown & Czeisler, 1992). Circadian analysis were not performed on melatonin data since melatonin samples were not collected during the daytime.

Missing data were replaced with the mean of the condition for that testing block. If more than one block for an individual was missing data for that subject were not used for analysis. Data are missing for the Digit Recall, Dual Task, PANAS, EEG, and circadian temperature analyses.

Due to difficulties in collecting EEG data without significant eye movement artifacts, spectral EEG data are not presented in this report. These difficulties were not expected as the problem was not experienced in previous studies.

To compensate for possible violations of repeated measure assumptions (e.g., sphericity, homogeneity of variance) and to decrease Type I error rate, Huyhn-Feldt Correction Factors were used in all analysis where appropriate. Modified Bonferroni Correction Factors were used to correct for multiple comparisons (Keppel, 1982). To equate groups at treatment onset, performance data

were transformed into change scores by subtracting the baseline score from all subsequent time points. For melatonin data, a log transformation (Log [x+1]) was also used to correct for heterogeneity of variance in the treatment comparisons. Original and transformed data are presented.

Results

To address the questions proposed in the current report, results will be presented for performance, alertness, mood, melatonin, and body temperature measures in three sections: Effects of Sleep Deprivation, Menstrual Cycle Phase (Follicular, Luteal), and Oral Contraceptive Use; Effects of Treatments (Caffeine, Bright Light); and Influence of Oral Contraceptive Use concerning Effects of Treatments.

Effects of Sleep Deprivation, Menstrual Cycle Phase (Follicular, Luteal), and Oral Contraceptive Use

These results evaluate the effects of menstrual cycle phase (follicular vs. luteal) and oral contraceptive use on women's responses to sleep deprivation and on circadian rhythms. Data are compared for women tested under Dim Light-Placebo conditions. Since the number of subjects available on Night 2 is small because of attrition, data for only Night 1 will be discussed. Data are described for the following conditions:

Dim Light Placebo-Follicular (DLP-FOL)	Dim Light Placebo-Luteal (DLP-LUT)	Dim Light Placebo-Oral Contraceptive (DLP-OC)

Alertness: Alertness levels decreased for all three Dim Light Placebo conditions across sleep deprivation. In general, small effects of menstrual cycle phase and oral contraceptive use on objective and subjective measures of alertness were observed during sleep deprivation.

During the nighttime hours, alertness in the follicular phase of the menstrual cycle was lower compared to women in the luteal phase and those using oral contraceptives. A significant Phase x Time-of-Night interaction [F (8,96) = 2.47, $p < .05$] and simple comparisons showed alertness was worse for the follicular phase during the last 3 hr testing block on Night 1 of sleep deprivation (Figure 1A). Alertness on the morning MWT between 0800 and 1000 hr was lowest for women in the luteal phase.

No effect of menstrual cycle phase (luteal vs. follicular) and oral contraceptive use on subjective sleepiness was observed (Figure 1B).

Performance: In general, performance on cognitive and reaction time based tasks degraded across sleep deprivation for women in all three Dim Light Placebo conditions. The lowest performance levels were observed between 0200 and 0800 hr (during the peak time of melatonin secretion and when temperature levels are low). Performance differences due to menstrual phase and oral contraceptive use were observed for several cognitive tasks. Generally, performance was lowest in the Follicular Phase. Performance for women in the luteal phase and women using oral contraceptives were similar across sleep deprivation.

Results for the 3 x 4 (Phase x Time of Night) repeated measure ANOVA analyses are provided in Table 3. Most tasks showed a main effect for Time of Night. Also, a few Phase and Phase x Time-of-Night interactions were obtained. Results for specific tasks are summarized next.

Women in the luteal phase of the menstrual cycle and women using oral contraceptives outperformed women in the follicular phase on 4 of 9 cognitive performance tasks during sleep deprivation (Figures 2A,2E,2F,2I). Also, performance was significantly better in women using oral contraceptives compared to women in the luteal phase for the continuous recognition task (Figure 2F), whereas luteal women outperformed oral contraceptive women for the Switching Task-Math Throughput (Figure 2A).

Simple and complex reaction time performance worsened for all groups during sleep deprivation. Reaction time performance tended to be best in the luteal phase for the Wilkinson Four Choice Reaction Time Task (Figure 2K) whereas Psychomotor Vigilance performance was not affected by menstrual cycle phase or the use of oral contraceptives (Figure 2J).

Mood: With the exception of Anger-Hostility, subjects' mood and vigor worsened across sleep deprivation (Figures 3A-3F). As evident in the figures, the effect of menstrual cycle phase (luteal vs. follicular) and oral contraceptive use on Tension-Anxiety, Vigor-Activity, Anger-Hostility, and Depression-Dejection mood scales were minimal. However, mood scores for Confusion-Bewilderment and Fatigue-Inertia were highest in the luteal phase the end of Night 1 (Figures 3B,3E).

Melatonin and Temperature: Hourly melatonin data from 2000 to 1000 hr for the 3 Dim Light-Placebo Conditions are presented in Figures 4A and 4B. As seen, oral contraceptives had some effect on melatonin levels. The Phase x Time-of-Night interaction, however, was nonsignificant $F(22, 264) = 1.65$, $p = .12$. Simple effects showed melatonin levels to be higher in oral contraceptive users.

Temperature levels were highest in women using oral contraceptives, intermediate in the luteal phase and lowest in the follicular phase (Figure 5A). Significant Phase [$F(2,24) = 4.07$, $p < .05$ and Phase x Time of Night [$F(22,264) = 26.63$, $p < .0001$] effects were observed. Simple comparisons confirmed phase differences (Figure 5A). The latter effects were observed across 24 hr (Figure 5B). Circadian temperature amplitude and phase were similar between groups whereas Mesor scores were significantly higher in women using oral contraceptives [$F(2, 21) = 3.83$, $p < .05$; Table 4].

Table 3. Analysis of variance summary for 3 x 4 (Menstrual Phase x Time of Night) repeated-measures analysis.

Task	Measure	F Phase (P) [2,24]	F Time of Night(TON) [3,72]	F P x TON [6,72]
Switching Task	Math Throughput	4.63*	2.44(.07)	2.82*
Two Column Addition	Throughput		6.04***	
Digit Recall	Throughput		6.83***	
Reaction Time Task	Throughput		19.51****	1.98(.08)
Dual Task	Throughput	4.04*	7.36***	2.41*
Continuous Recognition	Throughput	3.70*		
Probed Forced Memory Recall	Combined Associates		5.84***	
Dual Task	Control Losses		7.78***	
Switching Task	Mannequin Throughput			1.91(0.10)
Modified Psychomotor Vigilance Task	Reaction Time		65.98****	
Wilkinson Four Choice Reaction Time	Throughput		41.26****	1.89(.094)

Notes. Values in parentheses represent p values: *p < .05, **p < .01, ***p < .001, and ****p < .0001. Degrees of freedom for Digit Recall are [3,69].

Table 4. Circadian temperature values for the Dim Light Placebo conditions.

Group	Temperature Amplitude	Temperature Mesor	Phase Temperature Minimum Clock Time
Dim Light Placebo Oral Contraceptives n = 7	.22 ± .02	37.43 ± .06	04.36 ± .36
Dim Light Placebo Luteal n = 10	.22 ± .02	37.34 ± .08	04.26 ± .34
Dim Light Placebo Follicular n = 7	.25 ± .02	37.14 ± .05 ●	04.14 ± .25

Notes. ● = difference from Dim Light Placebo Oral Contraceptive group ($p < .05$).

Effects of Treatments (Caffeine, Bright Light)

These results describe the effects of sleep deprivation, caffeine, and bright light on women regardless of menstrual phase and oral contraceptive use. The effectiveness of caffeine and bright light treatments for increasing alertness and performance and for modifying the circadian rhythms of melatonin and temperature during 48 hr of sustained wakefulness are described for the following conditions:

Dim Light Placebo (DLP)	Bright Light Placebo (BLP)
Dim Light Caffeine (DLC)	Bright Light Caffeine (BLC)

If the pattern of results for the caffeine and bright light treatments differed significantly for women in the luteal phase compared to women using oral contraceptive, the differences are discussed.

Alertness: The effect of bright light and caffeine on objective and subjective measures of alertness during sleep deprivation will be examined next. In general, alertness was worse in the placebo conditions. Caffeine maintained higher levels of nighttime alertness compared to placebo and the Bright Light Caffeine condition produced the greatest alertness level of any conditions.

Dim Light Caffeine (Nights 1 and 2) and Bright Light Placebo (Night 2) improved alertness (MWT) relative to dim light placebo control (Figure 6A). The most marked effects on objective alertness, however, were observed in the combined Bright Light Caffeine condition. As seen in Figure 6A, alertness was highest in the combined treatment condition, especially on Night 2 of sleep deprivation. Significant main effects for Caffeine [$F(1,48) = 18.65$, $p < .0001$], Light [$F(1,48) = 5.79$, $p < .05$], and Night [$F(1,48) = 135.88$, $p < .0001$]; as well as Caffeine x Night [F

(1,48) = 12.82, $p < .001$]; and Light x Night [F (1,48) = 10.51, $p < .01$] interactions were observed for MWT data. In addition, interactions for Caffeine x Time of Night (Night 1) and Light x Time of Night (Night 2) occurred ($p < .05$). Average sleep latencies were significantly shorter on Night 2 than on Night 1 for all conditions except Bright Light Caffeine (Table on Figure 6A) Simple comparisons confirmed the alerting effects of caffeine and bright light (Figure 6A).

The morning MWT also showed significant main effects of Caffeine [Morning 1: F (1,48) = 32.53, $p < .0001$, Morning 2: F (1,48) = 13.34, $p < .001$] and Light [Morning 2: F (1,48) = 8.49, $p < .01$]. These tests show significantly improved alertness for both caffeine conditions on Morning 1 and the Bright Light Caffeine on Morning 2 (Figure 6A).

Figure 6B provides SSS data every 3 hr for each treatment condition on both nights. As seen, subjective sleepiness increased with sleep deprivation. The caffeine and light treatments showed less subjective sleepiness than the Dim Light Placebo condition on Night 1 whereas on Night 2, the effects of the treatments on subjective sleepiness are small. Simple comparisons show significant effects between the caffeine and placebo conditions (Figure 6B).

Performance: The effect of bright light and caffeine on performance during sleep deprivation will be examined first. In general, performance was worse in the Dim Light Placebo conditions. Caffeine and bright light treatments improved performance for both cognitive and reaction time based tasks during sleep deprivation. Significant effects of the caffeine treatments were observed for all 11 performance tasks relative to Dim Light Placebo. Also, performance was better in the Bright Light Placebo condition compared to Dim Light Placebo for 4 tasks and worse for one task. Overall, the caffeine treatments maintained high levels of performance across both nights of sleep deprivation, whereas the Bright Light Placebo condition enhanced performance relative to Dim Light Placebo on Night 2. Subjects receiving caffeine alone frequently outperformed those receiving bright light alone. In addition, the combination of bright light and caffeine tended to produce better performance than either caffeine or bright light alone for several tasks. Even

though caffeine and light treatments improved performance relative to dim light placebo, performance for most tasks was worse on Night 2 compared to Night 1 of sleep deprivation. There were, however, two tasks which showed significantly improved performance on Night 2 - Switching Task Mannequin Throughput and Continuous Recognition performance. Results of the 2 x 2 x 2 (Caffeine x Light x Night) ANOVA analyses for each task are provided in Table 5. As seen, most tasks showed a main effect for Caffeine and for Night. Also, a few Caffeine x Night and Light x Night interactions were obtained. Analysis for each night separately also revealed significant Caffeine x Time-of-Night, Light x Time-of-Night or Caffeine x Light x Time-of-Night interactions for all performance measures ($p < .05$) except Continuous Recognition. Generally, these data (Figures 7A-7K) show the light and caffeine treatments enhanced performance especially during the early morning (0200 to 0800 hr) when melatonin is peaking and temperature is low. Results for specific types of performance are summarized next.

Figures 7A through 7I present data for various tests of cognitive performance. As seen, nighttime performance was better for the caffeine versus the placebo conditions; especially during the early morning hours. In addition, the Bright Light-Placebo condition showed significantly better performance compared to the Dim Light Placebo condition for several tasks on Night 2. The Bright Light Caffeine condition also showed better cognitive performance compared to the Dim Light Caffeine on 3 of the cognitive performance tasks (Figures 7A,7B,7I). These differences were,however, significant only for the Switching Task Mannequin throughput performance on Night 1. There was also a trend for better Digit Recall performance in the Dim Light Caffeine versus Bright Light Caffeine condition.

Table 5. Analysis of variance summary for 2 x 2 x 2 (Caffeine Condition x Light Condition x Night) repeated-measures analysis.

Task	Measure	df	F Caffeine (C)	F Light (L)	F Night (N)	F C x L	F C x N	F L x N	F C x L x N
Switching Task	Math Throughput	1,48	7.57*						
Two Column Addition	Throughput	1,48	3.90 (.054)		26.78****				
Digit Recall	Throughput	1,46	8.06**		12.02***				
Reaction Time Task Time Uncertainty Block	Throughput	1,48			47.62****				
Dual Task	Throughput	1,47			30.40****				
Continuous Recognition	Throughput	1,48			33.45****				
Probed Forced Memory Recall	Combined Associates	1,46			6.55*		4.43*		9.94**
Dual Task	Control Losses	1,47			39.12****				
Switching Task	Mannequin Throughput	1,48	11.40*		10.71*			3.47 (.068)	
Modified Psychomotor Vigilance Task	Reaction Time	1,48	13.48****		91.91****				
Wilkinson Four Choice Reaction Time	Throughput	1,48	5.81*		43.16****				

Notes. Values in parentheses represent p values of trends: *$p < .05$, **$p < .01$, ***$p < .001$, and ****$p < .0001$.

In general, reaction time and psychomotor vigilance performance was better for the caffeine versus placebo conditions (Figures 7J,7K); especially during the early morning hours (between 0200 and 0800 hr). Caffeine improved simple reaction time performance on the Modified Psychomotor Vigilance Task better than exposure to bright light (Figure 7J). On Night 2, however, bright light exposure improved complex reaction time on the Wilkinson Four Choice as well as did caffeine after 2300 hr (Figure 7K).

Mood: The scores of all six sub-scales of the POMS changed as a result of sleep deprivation (Figures 8A-8F). Anger-Hostility, Depression-Dejection, Confusion-Bewilderment, Tension-Anxiety, and Fatigue-Inertia, increased whereas Vigor-Activity decreased. In general, little systematic effect of the treatments on mood are seen. The Bright Light Caffeine condition did, however, show less fatigue, more vigor and more anger at several times compared to one of the other treatments (differences vary for each mood measure).

As noted, the PANAS test was introduced midway through the study. Therefore the number of subjects in each condition is smaller than for the other measures (Figures 9A-9B). As evident in the Figures, positive affect decreased while negative affect increased as a result of sleep deprivation (Main effect of Night: Positive Affect, $F(1,35) = 85.85$, $p < .0001$; Negative Affect, $F(1,48) = 18.65$, $p < .0001$). Also, a significant interaction for Negative Affect (Caffeine x Night: $F(1,35) = 8.33$, $p < .01$) was observed. The Bright Light Placebo condition showed the lowest scores of positive affect (Night 1 and 2) and highest scores of negative affect (Night 2) during sleep deprivation. Positive and negative affect scores were similar in the Dim Light Caffeine, Bright Light Placebo and Dim Light Placebo conditions (Figure 9A,9B).

Melatonin and Temperature: Figures 10 and 11 show the bright light treatments reduced melatonin levels relative to the dim light conditions. However, exposure to 5,000 lux of bright light was not able to completely suppress melatonin the entire night. That is, during the latter portion of the night, especially on Night 2, melatonin levels rose during the bright light treatment. Dim Light Caffeine appeared to delay the onset of melatonin relative to the Dim Light Placebo condition on Night 1 (Figure 10A,11A). On Night 2, caffeine appeared to have no effect

on melatonin onset (Figure 10B,11B). Results for the Caffeine x Light x Night ANOVA using melatonin area under the curve data on the raw scores from 2100 to 0800 hr, showed main effects of Light [F (1,48) = 77.92, $p < .0001$] and Night [F (1,48) = 13.61, $p < .001$] and an interaction for Light x Night [F (1,48) = 4.37, $p < .05$]. A 2 x 2 x 12 (Caffeine x Light x Time of Night) ANOVA for each night also revealed main effects for Light and Time of Night both nights and interaction effects for Light x Time of Night (Nights 1 & 2), and Caffeine x Light x Time of Night (Night 1) (all $p < .05$). Trends for interactions for Caffeine x Time of Night (p = .07) and Caffeine x Light x Time of Night (p = .077) on Night 2 were also observed. Simple comparisons confirmed that melatonin levels in the Bright Light Placebo and Bright Light Caffeine conditions were lower than melatonin levels in the dim light conditions (Figures 10,11). There was a trend for reduced melatonin levels at the beginning of the night when comparing the Dim Light Caffeine to Dim Light Placebo condition. The effects of the caffeine treatments on melatonin levels differed for women in the luteal phase compared to women using oral contraceptives. Specifically, melatonin onset was delayed in the Dim Light Caffeine compared to the Dim Light Placebo condition for women in the Luteal Phase, whereas no such difference was observed for the same conditions in women using Oral Contraceptives (Figures 12A,12B) Bright Light treatment suppressed melatonin levels to a similar extent in women using and not using oral contraceptive agents.

In general, the Caffeine and Bright Light treatments attenuated the nighttime drop in body temperature compared to Dim Light Placebo (Figures 13A-13B). On Night 1, the combined treatment of Caffeine and Bright Light produced the most marked effects on temperature. As seen, the combined treatment condition maintained high temperature levels across the night. Bright Light Placebo maintained higher temperature levels compared to Dim Light Placebo on both nights whereas, on Night 2, caffeine had less of an effect on temperature (Figure 13B). Significant effects of Light [F (1,48) = 4.15, $p < .05$], Night [F (1,48) = 47.66, $p < .0001$] and Caffeine x Night [F (1,48) = 19.42, $p < .0001$] confirm these results. In addition to the latter effects, analyses for each night separately showed main effects of Light (Night 1) and Time of Night (Night 1 & 2), as well as interaction effects of Caffeine x Time of Night (Night 1) and

Light x Time of Night (Nights 1 & 2); all $p < .05$. Simple comparisons confirm temperature to be higher in caffeine and bright light treatments than the Dim Light Placebo condition (Figures 13A,13B). Moreover, the combined treatment of Bright Light Caffeine produced significantly higher temperature levels than either Bright Light or Caffeine alone. On night 2, the bright light conditions produced significantly higher temperature levels compared to the dim light conditions.

Similar to melatonin, an examination of bright light and caffeine treatments separately for women in the luteal phase compared to women using oral contraceptives reveals a different pattern of results for temperature measures. Specifically, Figures 14A and 14B show the treatments had larger effects on temperature relative to Dim Light Placebo for women in the luteal phase versus women using oral contraceptives.

In addition to the analysis of nighttime temperature levels, circadian temperature amplitude and mesor values were examined during, not subsequent to the light and caffeine treatments. Phase values could not be reliably determined due to small amplitudes in some subjects and are therefore not reported. Figures 15A through 15D show temperature levels every half hour across the 48 hr sleep deprivation period for each treatment. As seen in Figure 15A, the Dim Light Placebo and Dim Light Caffeine conditions showed the typical circadian rhythm in body temperature with a peak in the late afternoon and nadir in the early morning hours. The Bright Light Placebo and Bright Light Caffeine conditions showed relatively high temperatures across the 48 hr period. Results from the circadian analyses showed main and interaction effects for the treatments on amplitude and mesor scores (Table 6). The amplitude of the temperature rhythm on Night 2 was lower in the bright light versus dim light conditions. Also, temperature mesor was significantly higher for Bright Light Caffeine compared to all other conditions on Night 1 (Table 7).

Table 6. Analysis of variance summary for 2 x 2 x 2 (Caffeine Condition x Light Condition x Night) repeated-measures analysis.

Measure	df	F Caffeine (C)	F Light (L)	F Night (N)	F C x L	F C x N	F L x N	F C x L x N
Amplitude	1, 38		17.14 ***	3.71 (.06)		3.60 (.065)	10.75 **	
Mesor	1, 38			19.55 ****		6.87 **	4.83 *	

Notes. Values in parentheses represent p values of trends: *p < .05, **p < .01, ***p < .001, and ****p < .0001.

Table 7. Circadian temperature values for caffeine and bright light treatments.

Group	Temperature Amplitude	Temperature Mesor
Dim Light Placebo		
Day 1	0.21 ± .01	37.37 ± .07
Day 2	0.25 ± .02	37.38 ± .07
Bright Light Placebo		
Day 1	0.13 ± .02	37.42 ± .06 ■
Day 2	0.09 ± .01 *Δ	37.35 ± .06
Dim Light Caffeine	n	
Day 1	0.16 ± .02	37.38 ± .09 ■
Day 2	0.26 ± .05 ■	37.31 ± .08 ■
Bright Light Caffeine		n
Day 1	0.15 ± .03	37.52 ± .06 *
Day 2	0.15 ± .03 *	37.41 ± .06

Note. * = significantly different from DLP; Δ = significantly different from DLC; ■ = significantly different from BLC; and n = significant effect of Night.

Influence of Oral Contraceptive concerning

Effects of Treatments

These results examine whether oral contraceptive use influenced the effectiveness of the caffeine and bright light treatments to modify alertness, performance, and circadian rhythms in sleep deprived women. Data are described for the following conditions:

Dim Light Caffeine - Luteal (DLC-LUT)	Bright Light Placebo - Luteal (BLP-LUT)	Bright Light Caffeine - Luteal (BLC-LUT)
Dim Light Caffeine - Oral Contraceptive (DLC-OC)	Bright Light Placebo - Oral Contraceptive (BLP-OC)	Bright Light Caffeine - Oral Contraceptive (BLC-OC)

Comparisons for Dim Light Placebo - Luteal and Dim Light Placebo - Oral Contraceptives were presented above.

Alertness: Objective alertness (MWT) and subjective sleepiness (SSS) levels within each bright light and caffeine treatment were similar for women using and not using oral contraceptives across sleep deprivation (Figures 16,17).

Performance: Within each treatment condition, cognitive and reaction time based performance were similar for women taking and those not taking oral contraceptives. When differences in performance occurred, no systematic effect of oral contraceptives were observed. That is, performance was better for some tasks and worse for others when comparing women using oral contraceptives to women in the luteal phase across the caffeine and bright light treatments.

Caffeine and bright light treatments generally produced similar cognitive performance levels in women taking and not taking oral contraceptives (Figures 18-26). Notable differences among oral contraceptive users and nonusers were observed for two tasks under the Dim Light Caffeine treatment condition. Specifically, performance for the Dual Task – Control Loss measure was better in women in the luteal phase than in those using oral Contraceptives (Figure 25), whereas performance on the Continuous Recognition - Throughput measure (Figure 23) was better in women using oral contraceptives compared to women in the luteal phase. The Dual Task showed an interaction effect for Luteal-Oral Contraceptive Group x Time of Night [F (3,42) = 3.16, $p < .05$], and the Continuous Recognition task showed a main effect of Luteal-Oral Contraceptive Group (F (1,14) = 4.62, $p < .05$). Significant comparisons are shown on (Figures 23,25). There were also several non significant trends for better performance for women in the luteal phase compared to oral contraceptive users. A trend for the Digit Recall task under the Bright Light Placebo condition (Luteal-Oral Contraceptive Group x Time of Night, F (3,42) = 2.40, $p = .08$) and for the Probed Forced Memory Recall task under the Dim Light Caffeine condition (Luteal-Oral Contraceptive Group, F (1,14) = 3.60, $p = .08$) was observed.

Reaction time based performance were similar for women using and not using oral contraceptives under the caffeine and bright light treatments (Figures 27,28). There were, however, several nonsignificant trends of oral contraceptive use on Wilkinson - Throughput performance. Performance under the Bright Light Caffeine condition for the Wilkinson task tended to be better for women in the luteal phase compared to women using oral contraceptives whereas, under the Dim Light Caffeine condition, performance tended to be better for women using oral contraceptives compared to women in the luteal phase. Trends for interactions of Luteal-Oral Contraceptive Group x Time of Night were observed in the Bright Light Caffeine [F (3,42) = 2.65, $p = .089$] and Dim Light Caffeine [F (3,42) = 2.65, $p = .052$] conditions.

Mood: In general, women's mood levels within each bright light and caffeine treatment during sleep deprivation were similar for oral contraceptive users and women in the luteal phase. The Confusion-Bewilderment dynamic (Figure 29N), however, showed a significant Luteal-Oral

Contraceptive Group effect under the Bright Light Placebo condition, [F (1,14) = 4.85, $p < .05$] with higher scores for women in the luteal phase. No other effects or trends were observed for POMS data. Data for the Positive Affective Negative Affective Scale (PANAS) are not provided due to the small number of subjects available for comparison.

Melatonin and Temperature: Melatonin and temperature levels within each bright light and caffeine treatment condition were similar for the oral contraceptive luteal phase conditions (Figures 30-32). No differences were observed for any melatonin or temperature measure.

Discussion

Summary of Research Findings

Sleep deprivation, menstrual cycle phase, oral contraceptive use, and experimental treatment condition affected melatonin, temperature, alertness, performance, and mood in women. Specifically, sleep deprivation decreased alertness/performance and changed mood but did not affect melatonin and temperature. Menstrual cycle phase affected temperature, alertness/performance, and mood (fatigue) in that levels for all measures were generally higher in women during the luteal phase. Oral contraceptive use affected melatonin and temperature in that levels for both measures were higher in women taking oral contraceptives relative to women not taking oral contraceptives. However, alertness/performance was higher only relative to women in the follicular phase and mood (fatigue) was better only relative to women in the luteal phase. The treatments also affected the dependent measures of the study. Both caffeine ingestion and bright light exposure reduced melatonin and enhanced temperature. In addition, both of these treatments increased alertness/performance. In general, the combination of the two treatments was more effective than either treatment alone.

Circadian rhythms were evident in women across sleep deprivation, menstrual cycle phase, oral contraceptive use, and experimental treatment condition. Caffeine ingestion delayed melatonin onset in women while bright light exposure decreased temperature amplitude and increased temperature mesor.

In general, the data obtained in women were similar to that obtained in men (e.g., Badia et al., 1995; Wright et al., 1997a, 1997b). However, some differences were observed. Melatonin levels of women in the follicular phase were more similar to men than the melatonin levels of women in the other conditions. In addition, the melatonin levels of women in the luteal phase after caffeine ingestion were more similar to those of men after caffeine ingestion than the melatonin levels of women taking oral contraceptives. While the alertness/performance levels of women and men were similar, the effectiveness of the most potent treatment condition (i.e., combination of caffeine ingestion and bright light exposure) was less (relative to the other treatments) in women. Finally, the attrition rate tended to be higher in the study testing women (especially in the oral contraceptive condition) than in the study testing men.

Overview

Sleep deprivation is associated with a degradation in alertness, performance, and mood (e.g., Badia et al., 1995; Colquhoun, 1984; Smith, 1992; Wright et al., 1997a; 1997b). These changes are most salient when cognitive decisions (such as those required by military leaders) are required (e.g., Anderson, 1988-1989; Badia et al., 1995). While there are several studies assessing the effects of sleep deprivation, nearly all of this research has tested only men. Our study, which not only tested women but also investigated the effects of menstrual cycle phase and oral contraceptive use, is therefore unique. There have been a few previous studies testing the effects of sleep deprivation in women (Akerstedt & Froberg, 1977; Angus et al., 1985; Goodman et al., 1989; 1990). In general, the results of our study are consistent with the results of the latter studies. However, the present study exceeds these previous investigations in that both behavioral and physiological measures were assessed during different phases of the menstrual

cycle and in women taking, and not taking, oral contraceptives. In addition, the effects of caffeine ingestion and bright light exposure on behavioral and physiological measures were assessed.

Effects of Sleep Deprivation in Women on:

Alertness and Performance: The results of our study indicate that alertness (MWT; SSS) and performance (various measures) decreased as the amount of sleep loss increased in women. These findings are consistent with those of our previous study in men (e.g., Badia et al., 1995) and with the literature including the few investigations that have tested women (Akerstedt & Froberg, 1977; Angus et al., 1985; Goodman et al., 1989; 1990).

Mood: The results also indicate that mood (POMS; PANAS) worsened as sleep loss increased. This finding is also consistent with that of our previous study in men (e.g., Wright et al., 1997a; 1997b) and the research of others in women (e.g., Akerstedt & Froberg, 1977).

Melatonin and Temperature: Melatonin and temperature levels during sleep deprivation were unchanged from Night 1 to Night 2. Previous studies addressing this issue are conflicting. While there are theoretical reasons to predict that melatonin will increase and temperature will decrease with sleep deprivation (e.g., Badia et al., 1992) and some data are consistent with this notion (e.g., Akerstedt et al., 1979; Murray et al., 1958; Salin-Pascual et al., 1988; reviewed in: Badia et al., 1992), the present study and others suggest little change in these measures with sleep deprivation.

Circadian Rhythms: Finally, the results indicate that melatonin and temperature rhythms did not change with increased sleep loss. This finding is consistent with those of previous studies from our laboratory (e.g., Badia et al., 1995) as well as those from other laboratories testing men. The latter study showed that the change in circadian rhythms

resulting from an amount of sleep deprivation similar to that used in the present study (40 hr) was equivalent to the assessment error and day-to-day variability (about 30 min).

Effects of Menstrual Cycle Phase (Follicular, Luteal) on:

Alertness, Performance, and Temperature: The results of our study show that alertness, performance, and temperature levels were higher in women in the luteal phase than women in the follicular phase. The temperature finding is surprising given our finding that melatonin levels in the follicular and luteal phases were not significantly different; however, it is compatible with the findings of Kattapong et al. (1995) and Webley et al. (1985). Our finding that alertness and performance were higher in women during the luteal phase than in women during the follicular phase is not surprising given that temperature was higher in the luteal phase and given that our previous research has shown a close association between temperature and alertness/performance in men (e.g. Badia et al., 1995).

Mood: The results also show that the fatigue scores on the POMS were higher in the luteal phase than in the follicular phase. This is a surprising result given the temperature, alertness, and performance findings discussed above.

Melatonin: No difference in melatonin levels across the follicular and luteal phases of the menstrual cycle was observed. The latter finding is consistent with some of the previous reports (Berga & Yen, 1990;**Brzezinski et al.,**1988; Fellenberg et al., 1982; Hamilton et al., 1988; McIntyre & Morse, 1990) but not all (Arendt, 1978; 1979; Birau et al., 1981; **Brzezinski et al.,** 1987; Brun et al., 1987; Hariharasubramanian et al., 1985; Law, 1986; Ronnberg et al., 1990; Webley & Leidenberger, 1986; Wetterberg et al., 1976; Wirz-Justice & Arendt, **1979).**
Most of the latter studies found higher melatonin levels in the luteal phase. While the reasons for this inconsistency are unclear, many of the previous studies (e.g., Wirz-Justice & Arendt, 1979; Wetterberg et al., 1976) measured melatonin at only a few clock times. Such a technique can produce spurious results due to differences in circadian phase (Brown & Czeisler, 1992; Brown

et al., 1997; Shanahan & Czeisler, 1991). A strength of the present study was that melatonin was sampled hourly from 2000 to 1000 hr on both Nights 1 and 2.

Circadian Rhythms: Finally, the results show neither a change in melatonin amplitude, mesor, onset, offset, or phase nor a change in temperature amplitude, mesor, or phase related to menstrual cycle phase (follicular, luteal). However, there was a trend for women in the luteal phase to have a higher temperature mesor than women in the follicular phase. The latter finding is consistent with previous studies (Cagnacci et al., 1996; Kattapong et al., 1995; Lee, 1988; Parry et al., 1997a; Severino et al., 1991). Our temperature phase finding is consistent with that of one study (Lee, 1988) but conflict with that of another (Cagnacci et al., 1996). The latter study found that women in the luteal phase have a later temperature trough than women in the follicular phase. Our melatonin amplitude finding does not agree with that of Parry et al. (1997b) which showed that women in the luteal phase have a smaller amplitude than women in the follicular phase. A smaller temperature amplitude in the luteal phase relative to the follicular phase has also been reported (Cagnacci et al., 1996; Kattapong et al., 1995; Lee, 1988; Parry et al., 1997a; Severino et al., 1991). The time of melatonin onset finding differs with that of Cagnacci et al. (1996) which revealed that women in the luteal phase have a later melatonin onset (and temperature trough) than women in the follicular phase. A probable reason for these differences is that most of the previous studies did not use a constant routine procedure (e.g., Cagnacci et al., 1996; Kattapong et al., 1995; Lee, 1988) as the present study did. Failure to use a constant routine affects the measurement of circadian rhythms (Brown & Czeisler, 1992; Brown et al., 1997; Czeisler & Jewett, 1990; Shanahan & Czeisler, 1991). However, it is possible that our results were affected by the fact that, for unknown reasons, not all women had elevated levels of progesterone in the luteal phase the day prior to testing.

Effects of Oral Contraceptive Use on:

Alertness and Performance: The results of our study indicated that alertness and performance were higher in women taking oral contraceptives than in women in the follicular phase. Higher

alertness and performance could be related to the higher temperature also observed in this group (see below). However, higher melatonin levels were also obtained in this group and other researchers have that higher melatonin is associated with lower alertness (e.g., Akerstedt et al., 1979). No other study has addressed this question.

Mood: The results also indicate that scores on the fatigue dynamic of the POMS were lower in women taking oral contraceptives than in women in the luteal phase but not different from women in the follicular phase. It is difficult to interpret this finding. However, it is consistent with reports of women beginning oral contraceptive use in that these women typically report less premenstrual symptoms after beginning to take oral contraceptives (Graham, 1989; Herzberg & Coppen, 1970).

Melatonin: Oral contraceptive use increased melatonin levels (relative to women not taking oral contraceptives). This finding is consistent with most (Arendt, 1978; 1979; Brun et al., 1987; Tapp et al., 1980; Webley & Leidenberger, 1986; Webley et al., 1985) but not all (Beck-Friis et al., 1984; Delfs et al., 1994) previous reports. Our results are also consistent with the anti-gonadal effects of exogenous melatonin shown in nonhumans (reviewed in: Cagnacci & Volpe, 1996). Reasons for the disparity in the studies testing humans are unknown. As noted, many studies assessed melatonin only at a few time points (Beck-Friis et al., 1984), a technique that can produce misleading results (Brown & Czeisler, 1992; Brown et al., 1997; Shanahan & Czeisler, 1991).

Temperature: The results indicate that oral contraceptive use increased temperature levels (relative to women not taking oral contraceptives. This finding likely occurred due to the synthetic progesterone, a hyperthermic agent (e.g., Little et al., 1974), present in the oral contraceptives (Israel & Schneller, 1950; Mouzon et al., 1984). Some researchers have observed higher body temperatures associated with oral contraceptive use (Webley et al., 1985), but others have not observed temperature differences in women taking, and not taking, oral contraceptives during the pseudo-luteal and luteal phases (Kattapong et al., 1995). Results of the latter study revealed

differences between the two groups (i.e., women taking and not taking oral contraceptives) during the pseudo-follicular and follicular phase, however.

Circadian Rhythms: Finally, the results indicate neither a change in melatonin amplitude, mesor, onset/offset, or phase nor a change in temperature amplitude or phase as a function of oral contraceptive use. However, we did note that temperature mesor was higher in women taking oral contraceptives relative to women in the follicular phase but not different from women in the luteal phase. The latter finding is consistent with that of another study (Severino et al., 1991). Our melatonin finding contrasts that of another study (Reinberg et al., 1996) which showed oral contraceptive use **"obliterated"** the melatonin rhythm. A probable reason for this discrepancy relates to the infrequent sampling rate of the Reinberg et al. study; that is, the sampling rate of the Reinberg et al. study was not sufficient to detect a circadian rhythm in melatonin.

Taken together, the above results may appear paradoxical. Higher melatonin levels should be associated with lower temperature levels (e.g., Badia et al., 1992) and lower alertness/performance levels. However, the increase in body temperature levels associated with oral contraceptive use was apparently sufficient to offset the effects of the increase in melatonin associated with oral contraceptive use and alertness/performance were increased in this condition.

Effects of Treatments (Caffeine, Bright Light) on:

Alertness, Performance, Mood, Melatonin, and Temperature: The results of our study show that caffeine alone, bright light alone, as well as the combination of caffeine and bright light increased alertness, performance, and temperature during the nighttime hours in women. Bright light alone and the combination of caffeine and bright light also suppressed melatonin during the nighttime hours. Finally, bright light alone decreased positive affect and increased negative affect. In general, these results (obtained in women) are compatible with those (obtained in men)

in our previous study (e.g., Wright et al., 1997a; 1997b). In addition, the bright light findings are compatible with the results of others (e.g., Campbell & Dawson, 1990; French & Hannon, 1990). However, no previous study has assessed the effects of (a) caffeine/bright light on mood or (b) caffeine on melatonin in women or in men.

Circadian Rhythms: The results also show that the treatments affected melatonin onset (delayed by caffeine in women in the luteal phase), temperature amplitude (lower in bright light than in dim light collapsed across caffeine ingestion), and temperature mesor (higher in bright light than in dim light collapsed across caffeine ingestion. These results are consistent with our previous studies testing men (e.g.., Badia et al., 1995). No other study has assessed the effects of caffeine on circadian rhythms in women or in men.

It is important to note the advantages and disadvantages of the treatments tested in the present study (caffeine, bright light). Caffeine ingestion does not require equipment and thus allows more ambulatory behavior and more covert operation than does bright light exposure. However, the effects of caffeine may be more difficult to reverse than those of bright light. For example, the alertness- and performance-enhancing effects of caffeine can persist (and thereby disrupt sleep) for up to several hours after ingestion (Landolt et al., 1995). In contrast, the positive effects of bright light (on alertness and performance) can be reversed within minutes (e.g., Badia et al., 1991). In the present study, both treatments were associated with minor untoward effects (e.g., negative affect, stomach discomfort).

Influence of Oral Contraceptive Use concerning Effects of Treatments on:

Alertness, Performance, Mood, Melatonin, Temperature, and Circadian Rhythms: The results of our study indicate little influence of oral contraceptive use on the effects of the treatments. That is, oral contraceptive use and the experimental treatments generally did not

interact. An exception to this generalization is the finding that caffeine did not suppress melatonin in women taking oral contraceptives whereas it did in women in the luteal phase. Other researchers have shown that the use of oral contraceptives increases the amount of time necessary for caffeine to be eliminated from the circulation (e.g., Patwardhan et al., 1980; Rietveld et al., 1984). Given this fact and given the dose-response relationship for the effects of caffeine (i.e., larger amounts of caffeine are associated with larger effects) (e.g., Penetar et al., 1994), we expected women taking oral contraceptives to exhibit larger increases in alertness, performance, and temperature as well as larger decreases in melatonin in response to caffeine ingestion (relative to women not taking oral contraceptives). While no evidence of such an effect was observed in the present study, it is possible that our sample size was too small to detect such an effect.

Differences and Similarities in Women and Men concerning:

Effects of Sleep Deprivation: In general, the results of our studies show that women and men responded in a similar manner to sleep deprivation. An exception to this summary is the attrition rate: More women left the experiment early (see Appendix). Akerstedt and Froberg (1977) also noted that women were "more susceptible" to sleep deprivation. However, our finding concerning attrition should be interpreted cautiously as there were some differences in the protocols used to test the women and men. For example, women were more socially isolated during the constant routine: Women were tested individually (one woman in each testing room) whereas men were tested in pairs (two men in each testing room).

Effects of Treatments: The results also show that women and men responded in a similar manner to the treatments used to counter (i.e., countermeasures) the effects of sleep deprivation. For example, the melatonin levels of women in the luteal phase after caffeine ingestion were similar to those of men (i.e., melatonin was suppressed by caffeine). However, this finding was not evident in women in the oral contraceptive condition. A reason for this difference may

be that oral contraceptive use altered the response to caffeine ingestion; but, the finding may instead be a gender difference. If it is related to gender, a possible explanation for the differences in the effects of caffeine between women and men concerns dosing. In the present study, women were given one 100 mg capsule four times a night. In our previous study (e.g., Badia et al., 1995) men were given two 200 mg capsules two times a night. While the dose across the night was identical, the women weighed less than the men (on average). Larger doses of caffeine are more likely to be associated with untoward effects such as nausea (Stern et al., 1989). In addition, women were exposed to a higher intensity of light (5,000 lux) than men (2,500 lux). These protocol differences may relate to what appeared to be a greater attrition rate in the study testing women.

Circadian Rhythms: Finally, the results show that women and men exhibit similar circadian rhythms. However, oral contraceptive use affected the ability of caffeine to delay melatonin onset in women (relative to men). In addition, temperature rhythms (amplitude, mesor) of women in the follicular phase were most similar (of the conditions tested) to the data of men. This finding is corroborated by the results of another study (Kattapong et al., 1995).

Recommendations

Effects of Sleep Deprivation in Women

In the present study, alertness, performance, and mood worsened as the amount of sleep deprivation increased. In addition to degradation due to this "homeostatic" (hours awake) component, alertness, performance, and mood degraded due to a "circadian" (daily rhythmicity) component; that is, each measure troughed during the early morning hours (0200 to 0800 hr), a time when melatonin levels were highest and temperature levels lowest.

Given these findings, we recommend that military personnel be cognizant of the changes in alertness, performance, and mood associated with sleep deprivation and diurnal rhythmicity.

Effects of Treatments (Caffeine, Bright Light) in Women

Our laboratory and others have shown that most of the changes in alertness and performance associated with the homeostatic and circadian components can be attenuated by judicious use of countermeasures. These countermeasures include those effectively utilized in the present study (caffeine and bright light) as well as those used in our previous work and that of others. The latter countermeasures include prophylactic naps (e.g., Badia et al., 1995; Dinges et al., 1987; Bonnet, 1991; Rosekind et al., 1995) and nonsteroidal anti-inflammatory drugs (NSAIDS; e.g., ibuprofen) (e.g., Badia et al., 1995; Murphy et al., 1995; 1996).

Some of our data suggest that menstrual cycle phase and oral contraceptive use may modify the effectiveness of these treatments.

Given these findings, the treatments noted above should be considered whenever situations requiring extended wakefulness arise. However, additional research on their use is needed. In particular, further study of the effects menstrual cycle phase and oral contraceptive use on the responses of women to the treatments is warranted.

Limitations of Treatments in Women

Bright light exposure may be an effective countermeasure (in that it increases alertness and performance by suppressing melatonin and enhancing temperature); however, it may also decrease positive affect and increase negative affect.

Oral contraceptives use appears to have little effect on the responses of women to counter-measures (in that it did not modify the alertness- and performance- enhancing effects of caffeine and light); however, it may make women less tolerant to sleep deprivation [as women taking oral contraceptives tended to withdraw from the experiment more frequently than women tested in the other conditions and men tested previously [Badia et al., 1995)].

(This finding must be considered tentative given our sample size and given the procedural differences in the study testing women and that testing men.) As noted, women taking oral contraceptives had higher melatonin and this factor alone could place them at risk for increased sleepiness (e.g., Badia et al., 1992). However, the effect that the higher melatonin levels might have on women taking oral contraceptives may be offset by the higher temperature levels also exhibited by them. (Higher body temperatures are associated with increased alertness and performance; e.g., Badia et al., 1995). This notion (that the combination of the sleepiness-enhancing levels of melatonin and sleepiness-suppressing levels of temperature may counteract each other) may explain why levels of alertness and performance did not differ between women taking oral contraceptives and women in the luteal phase.

Caffeine ingestion may delay melatonin onset and it may thereby improve alertness, performance as well as mood, however; it may be most efficacious in women not using oral contraceptives.

Given these findings, we recommend that military personnel be aware that: (a) bright light may increase negative affect; (b) women taking oral contraceptives may be less tolerant to sleep deprivation; and (c) some treatment effects may be attainable only in certain women at certain times (e.g., women taking oral contraceptives tested during the pseudo-luteal phase).

However, again, we note that these recommendations must be considered tentative and further research is necessary to validate our findings. The latter notion is especially true concerning possible gender differences.

Differences and Similarities in Women and Men

In general, women and men (studied previously; e.g. Badia et al., 1995) responded to sleep deprivation and counter measures in similar manner. Women in the luteal phase appeared more responsive to caffeine ingestion (melatonin suppression) than women taking oral contraceptives.

Of the conditions tested, women in the luteal phase responded to caffeine ingestion in a manner most similar to that of men.

Given these findings, we recommend that military personnel be aware that, in general, women and men respond to sleep deprivation similarly. However, it is important to note that phase of the menstrual cycle phase and oral contraceptive use may affect the responses of women to extended wakefulness.

CONCLUSIONS

Sleep deprivation affected alertness, performance, and mood without affecting melatonin and temperature.

Alertness (MWT) and performance (in general) decreased and mood (POMS, PANAS) worsened as the amount of sleep deprivation increased. On both nights, alertness and performance were lowest and mood was worse between the hours of 0200 and 0800 hr.

Melatonin and temperature were unchanged from Night 1 to Night 2.

A circadian rhythm was observed in alertness, performance, mood, melatonin, and temperature.

Alertness, performance, mood, and temperature peaked during the day and troughed during the night. In contrast, melatonin peaked during the night and troughed during the day.

Menstrual cycle phase and oral contraceptive use affected alertness, performance, mood, melatonin, and temperature.

Alertness (MWT) and performance (in general) scores during the night were lowest in women

in the follicular phase (relative to women in the other two conditions). Alertness scores of women in the luteal phase and women taking oral contraceptives did not differ.

Mood scores (POMS) on the fatigue-inertia scale during the night were, in general, highest in women in the luteal phase (relative to women in the other two conditions). Mood scores of women in the follicular phase and women taking oral contraceptives did not differ.

Melatonin levels during the night were highest in women taking oral contraceptives (relative to women in the other two conditions). Melatonin levels of women in the follicular phase and women in the luteal phase did not differ.

Temperature levels during the day and night were highest in women taking oral contraceptives, intermediate in women in the luteal phase, and lowest in women in the follicular phase.

Menstrual cycle phase and oral contraceptive use did not affect circadian rhythms in alertness, performance, mood, melatonin, temperature.

As noted, alertness, performance, mood, and temperature peaked during the day and troughed during the night while melatonin peaked during the night and troughed during the day. Amplitude and phase of the circadian rhythm in temperature were similar across menstrual cycle phase and oral contraceptive use. The mesor was higher in women taking oral contraceptives relative to women in the follicular phase but not different from women in the luteal phase (who did not differ from women in the follicular phase).

Caffeine and bright light (administered separately and in combination during the nighttime hours) affected alertness, performance, mood, melatonin, and temperature.

Caffeine alone, bright light alone, as well as caffeine and bright light combined enhanced nighttime alertness (MWT) and performance (in general) [relative to the control condition

(i.e., the Dim Light Placebo group)]. Caffeine and bright light combined enhanced alertness to the greatest extent (relative to the other two treatments). Caffeine alone enhanced alertness and performance more than bright light alone.

Caffeine alone had little effect on nighttime mood. Bright light alone was associated with the highest scores of negative affect and the lowest scores of positive affect (PANAS) (relative to the other two treatments).

Caffeine alone suppressed nighttime melatonin but its effects were not as dramatic as those of bright light alone as well as those of caffeine and bright light combined [relative to the control condition (i.e., the Dim Light Placebo group)]. Bright light alone did not completely suppress melatonin during the latter part of the night; this finding was especially salient on Night 2.

Caffeine alone, bright light alone, as well as caffeine and bright light combined enhanced nighttime temperature [relative to the control condition (i.e., the Dim Light Placebo group)].

Caffeine and bright light affected circadian rhythms in melatonin and temperature.

Melatonin onset was delayed in the caffeine alone conditions (relative to the other conditions) in some subjects but not in others.

Temperature amplitude was lower, and temperature mesor was higher, in the bright light conditions (relative to the dim light conditions) collapsed across caffeine ingestion.

Caffeine and bright light (administered separately and in combination during the nighttime hours) had similar effects on temperature, alertness, performance, and mood, in women taking oral contraceptives and in women not taking oral contraceptives.

Caffeine and bright light: increased temperature, alertness, and performance; as well as

affected mood. These effects were similar in both groups (i.e., women taking, and not taking, oral contraceptives).

Caffeine alone delayed melatonin onset in women in the luteal phase (relative to women in the caffeine-oral contraceptive condition and to women in the placebo-oral contraceptive condition). Caffeine had little effect in women taking oral contraceptives (relative to women in the placebo-oral contraceptive condition).

Caffeine alone and bright light alone enhanced alertness (MWT) and performance (in general) in women.

Caffeine alone had little effect on mood (POMS, PANAS) in women. Bright light alone worsened mood.

Caffeine alone suppressed melatonin levels in women. However, this effect was evident in some subjects but not in others. Subsequent analyses revealed that the melatonin levels of women in the luteal phase after caffeine ingestion were similar to those of men after caffeine ingestion.

Similar to the data of men (studied previously; e.g., Badia et al., 1995; Wright et al., 1997a; 1997b), a circadian rhythm in alertness, performance, mood, melatonin, and temperature was evident in women.

Alertness, performance, mood, and temperature peaked during the day and troughed during the night. In contrast, melatonin peaked during the night and troughed during the day.

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APPENDIX

Background Information

The table on the next three pages shows background information for the subjects tested in the present experiment.

Background Information

Subject	Light	Caffeine	Menstrual Phase	Cycle Day of Blood Test	Progesterone Levels	Oral Contraceptives	Age	Weight	Height (in)	Morning Eveningness Q
103	DL	Placebo	Luteal	22	13.7	None	18	134	64	38
110	DL	Placebo	Luteal	18	6.3	None	19	111	63	24
127	DL	Placebo	Luteal	22	4.8	None	22	135	70	36
131	DL	Placebo	Luteal	15	0.5	None	20	153	63	27
140	DL	Placebo	Luteal	17	0.7	None	18	127	68	39
151	DL	Placebo	Luteal	23	1.0	None	24	145	64	36
162	DL	Placebo	Luteal	18	4.2	None	18	140	67	23
170	DL	Placebo	Luteal	20	6.1	None	18	140	65	23
173	DL	Placebo	Luteal	20	3.6	None	18	165	67	37
179	DL	Placebo	Luteal	18	2.5	None	19	123	62	31
191	DL	Placebo	Luteal	24	12.1	None	18	125	64	29
Average				19.7	5.0		19.3	136.2	65.2	31.2
106	DL	Caffeine	Luteal	16	0.4	None	19	109	61	35
117	DL	Caffeine	Luteal	20	0.7	None	18	115	64	40
125	DL	Caffeine	Luteal	19	7.6	None	22	128	64	21
132	DL	Caffeine	Luteal	23	13.1	None	26	109	62	40
139	DL	Caffeine	Luteal	18	13.9	None	19	122	64	39
146	DL	Caffeine	Luteal	17	2.8	None	20	115	64	30
163	DL	Caffeine	Luteal	19	11.3	None	21	105	64	23
165	DL	Caffeine	Luteal	22	5.9	None	18	127	67	32
Average				19.3	6.96		20.4	116.3	63.8	32.5
107	BL	Placebo	Luteal	17	12.4	None	20	117	63	25
114	BL	Placebo	Luteal	22	8.4	None	18	126	62	34
121	BL	Placebo	Luteal	18	7.7	None	18	123	65	35
128	BL	Placebo	Luteal	20	15.4	None	19	155	64	25
145	BL	Placebo	Luteal	18	1.4	None	18	130	66	27
147	BL	Placebo	Luteal	19	6.2	None	19	120	66	24
158	BL	Placebo	Luteal	18	1.0	None	21	102	63	31
169	BL	Placebo	Luteal	19	2.8	None	21	135	65	31
Average				18.9	6.91		19.3	126.0	64.3	29.0

Subject	Light	Caffeine	Menstrual Phase	Cycle Day of Blood Test	Progesterone Levels	Oral Contraceptives	Age	Weight	Height (in)	Morning Eveningness Q
108	BL	Caffeine	Luteal	19	1.6	None	19	105	65	38
113	BL	Caffeine	Luteal	23	0.3	None	18	142	64	32
124	BL	Caffeine	Luteal	20	4.8	None	18	126	65	33
134	BL	Caffeine	Luteal	20	3.2	None	18	128	63	29
143	BL	Caffeine	Luteal	18	4.3	None	21	125	68	43
157	BL	Caffeine	Luteal	23	14.8	None	22	115	62	32
164	BL	Caffeine	Luteal	18	12.0	None	18	128	66	30
183	BL	Caffeine	Luteal	22	2.5	None	19	145	69	38
Average				20.4	5.44		19.1	126.8	65.3	34.4
112	DL	Placebo		18	0.5	Ortho-Cyclen 28	22	110	62	30
119	DL	Placebo		18	0.3	Ortho Tri-Cyclen	21	121	63	30
138	DL	Placebo		18	0.1	Desogen	18	140	64	38
148	DL	Placebo		18	0.4	Triphasil	19	120	64	30
149	DL	Placebo		18	0.4	Ortho-Novum 7/7/7	19	125	64	35
175	DL	Placebo		25	0.5	Norethin 1/35E	19	115	58	33
184	DL	Placebo		16	0.5	Desogen	21	150	66	28
196	DL	Placebo		18	0.8	Tri-Levlen	20	172	67	45
Average				18.6	0.44		19.9	131.6	63.5	33.6
104	DL	Caffeine		18	0.2	Ortho-Cept	19	131	64	32
115	DL	Caffeine		17	0.2	Triphasil	22	159	65	25
126	DL	Caffeine		18	0.2	Triphasil 28	20	170	63	43
135	DL	Caffeine		18	0.3	Nordette	21	140	65	21
141	DL	Caffeine		19	0.6	Ortho-Novum	20	148	68	33
155	DL	Caffeine		18	0.3	Ortho-Novum 7/7/7	19	150	64	27
172	DL	Caffeine		18	0.2	Ortho-Cept	21	157	64	29
178	DL	Caffeine		18	0.4	Triphasil	19	163	62	31
Average				18.0	0.30		20.1	152.3	64.4	30.1

Subject	Light	Caffeine	Menstrual Phase	Cycle Day of Blood Test	Progesterone Levels	Oral Contraceptives	Age	Weight	Height (in)	Morning Eveningness Q
102	BL	Placebo		18	0.2	Triphasil	24	145	65	32
116	BL	Caffeine		19	0.8	Ortho-cyclen	18	135	69	31
123	BL	Placebo		16	0.5	Ortho-Cept	20	130	63	31
130	BL	Placebo		18	0.5	Ortho-Cept	20	155	64	35
137	BL	Placebo		18	0.7	Orthocyclen	20	125	66	49
154	BL	Placebo		18	0.5	Ortho-Novum 7/7/7	20	155	70	23
167	BL	Placebo		18	0.6	Ortho-Cyclen	20	155	66	30
193	BL	Placebo		18	1.0	Demulin 1/35-28	18	149	69	24
Average				17.9	0.60		20.0	143.6	66.5	31.9
109	BL	Caffeine		18	0.6	Levlen 28	20	124	66	44
111	BL	Caffeine		18	0.6	Ortho-Cept	19	120	62	27
122	BL	Caffeine		18	0.3	Ortho-Novum 7/7/7	19	160	66	21
133	BL	Caffeine		18	0.7	Ortho-Cept	20	115	61	32
152	BL	Caffeine		18	0.3	Ortho-Cyclen	19	161	65	32
159	BL	Caffeine		18	0.4	Ortho Tri-Cyclen	19	127	65	31
166	BL	Caffeine		18	0.5	Lo/ovral	19	140	65	31
194	BL	Caffeine		21	0.3	Tri-Cyclen	18	128	63	42
Average				18.4	0.46		19.1	134.4	64.1	32.5
101	DL	Placebo	Follicular	7	0.3	None	25	140	67	37
118	DL	Placebo	Follicular	9	0.5	None	20	135	66	29
120	DL	Placebo	Follicular	5	0.6	None	20	130	65	22
129	DL	Placebo	Follicular	10	0.7	None	22	112	65	37
142	DL	Placebo	Follicular	11	0.5	None	18	130	66	23
153	DL	Placebo	Follicular	8	0.7	None	21	165	65	36
161	DL	Placebo	Follicular	7	0.7	None	21	112	61	41
168	DL	Placebo	Follicular	9	0.8	None	18	130	68	19
Average				8.3	0.60		20.6	131.8	65.4	30.5

Reasons People were Excluded from Participation

Reason(s)	Number	Percentage
Multiple Reasons (from the list below)	694	53
Medical & Medication Use	130	10
Sleep Schedule/Sleep Problems	53	04
Caffeine Intake (mostly too low)	226	17
Cigarette Smokers	84	06
Lack of Menstrual Cycle Regularity	41	03
Weight (mostly too heavy)	48	04
Pregnancy	00	00
English not 1st language	15	01
Dietary Problems	25	02
Excessive Consumption of Alcohol	3	< 01
Other	3	< 01

Number not Meeting Criteria	1322
Number Meeting Criteria but Later Declined to Participate	149
Number Tested	98
Total Screened	1569

Reasons for Losing Participants during the Study

Seventeen subjects were terminated between Wednesday's blood testing and the beginning of the sleep deprivation period Friday morning. After the beginning of the sleep deprivation period, 4 subjects terminated prior to completing one night of sleep deprivation and 2 subjects were removed due to violation of the experimental protocol or experimental error. Of the remaining 74 subjects, 15 subjects terminated participation after 1 night of sleep deprivation and a total of 59 completed both nights of the study. Reasons for leaving and negative side effects of the treatments are listed on the following page.

Subjects' Physical Symptoms

Subject #	Physical Complaint	Time of Departure
DLP-LUT		
127	Headache, Sleepiness	1100 Saturday
162	Sleepiness, Weak muscles	0700 Saturday
173	Sleepiness, Lack of motivation	2100 Saturday
DLC-LUT		
132	Missed Dose 8	
163	Fast pulse	1400 Saturday
BLP-LUT		
195	Did not eat	0800 Saturday
BLC-LUT		
108	Vomited, Headache	
DLP-OC		
112	Nausea, Dizziness, Sweating	0330 Sunday
148	Nausea	2400 Sunday
184	Migraine, Sleepiness	0315 Sunday
DLC-OC		
104	Lactose intolerant	0200 Saturday
115	Upset stomach	0100 Saturday
BLP-OC		
123	Vomited	0600 Saturday
156	Nausea, Heat, Headache	0130 Saturday
193	Headache, Upset stomach	1730 Saturday
BLC-OC		
109	Nausea, Diarrhea	0700 Sunday
111	OC Confusion	1800 Saturday
133	Nausea, Headache	0400 Sunday
144	Nausea	0030 Saturday
159	Nausea, Warm	0600 Saturday
194	Emotional, Dizziness, Headache	0700 Sunday
DLP-FOL		
118	Emotional	0745 Saturday

Difficulties Scheduling Subjects

We screened 1,569 women for the study. Of these people, 1,322 failed to meet the criteria below. One-hundred forty-nine passed the screening criteria but subsequently declined to participate. Ninety-seven subjects have been tested. Of the 97 subjects tested, data for at least one night of sleep deprivation is available for 75 individuals.

As previously noted, our rejection rate for the current study is around 85% whereas previous studies the rejection rate was lower being 75%. In addition, of those meeting the screening criteria in previous work, 92% have participated. In the current study, only 33% of individuals qualifying for the study have participated.

One specific reason that we had difficulty in scheduling participants for the study is because of the small window of opportunity in which to schedule women each month (i.e., Women using oral contraceptives can only be tested one weekend per month--beginning with day 20 ± 3 of their cycle the Wednesday prior to testing; Women not using oral contraceptives need to be tested beginning either day 20±3 or day 9±2). Schedule conflicts were common; potential subjects were frequently not available for testing on the weekend that their cycle fit into. This was less of a problem in the past when we tested men since we had more opportunities each month from which subjects could choose from.

Another difficulty with scheduling is the need to keep menstrual cycle logs for 1-2 months prior to participating and potential dates of testing at the beginning of most semesters were missed because this information was not yet available.

Performance Battery

The performance battery used in the current study is made up of tasks from the Walter Reed Performance Assessment Battery (Walter Reed PAB), the United Triservice Performance Assessment Battery (UTCPAB), and tasks from the sleep laboratories of the University of Pennsylvania and Bowling Green State University (Dinges et al., 1993; 1994; Gillooly, et al., 1990; Thorne, 1990; Thorne et al., 1985). A list of the tests is provided in the table below and a description of each task follows.

The performance battery requires reading and mathematical ability above the grade school level. No touch typing skills are required to perform the tasks, however normal dexterity of the hands and fingers as well as normal or corrected vision is necessary. Tests from the Walter Reed PAB and UTCPAB have been used for studying the effects of sleep deprivation, sustained performance, jet lag, heat stress, physical fatigue, physical conditioning, atropine, hypoxia, and sickle cell disorders (Thorne et al., 1985). Typically, normal, healthy, motivated young adults with a high school to college education have been examined with the performance battery. Tests from the University of Pennsylvania and modified by Bowling Green State University are relatively new, developed in the past few years, and have been used for studying the effects of sleep deprivation, sustained performance, and fatigue (Dinges et al., 1993; 1994).

List of Tasks and Measures

Dual Task	-- *Throughput, *Control Losses, RMS, Accuracy, Speed
Switching Task	-- *Math Throughput, Math Reaction Time, Math Mean Correct Reaction Time, *Mannequin Throughput, Mannequin Reaction Time, Mannequin Mean Correct Reaction Time,
Reaction Time Task (Time Uncertainty Block)	-- *Throughput, Accuracy, Speed, %incorrect, %lapses.
Continuous Recognition	-- *Throughput, %correct, Reaction Time
Two-Column Addition	-- *Throughput, Accuracy, Speed
Digit Recall	-- *Throughput, Accuracy, Speed
Probed Force Memory Recall	-- * Combined Associates Recalled, Strong Associates Recalled, Weak Associates Recalled
Wilkinson Four Choice Reaction Time	-- *Throughput, Accuracy, Speed
Modified Psychomotor Vigilance Task	-- *Reaction Time

Notes. Tasks underlined represent tasks from either the Walter Reed PAB or United Triservice PAB. Tasks not underlined represent relatively new tasks developed by research laboratories at the University of Pennsylvania and Bowling Green State University to study the effects of sleep deprivation, continuous performance, and fatigue.

* = measures statistically analyzed.

Description of Tasks

Dual Task: This test is a task of divided attention. Subjects are required to perform concurrently two tasks: Unstable Tracking and Memory Search. In the tracking task, the subjects objective is to keep a cursor centered on a target area in the middle of the monitor screen. The cursor is controlled by moving the mouse. The cursor initially appears on the central target, but tends to move horizontally away from this position. The subjects try to keep it centered over the target at all times. If it reaches the boundary line, it will reappear at the target position and begin moving away again. While subjects are controlling the cursor, they are required to respond to test letters in the memory search component of the task. Subjects are shown a "memory set" that contains two letters, which they are allowed to look at for as long as they wish. When they have memorized this set, they press one of the response keys and the tracking task begins immediately. After a few seconds, the memory set disappears and the subjects are shown a series of single test letters and must decide whether each test letter is one of the letters in the memory set. If subjects do not respond to a test letter within a certain time, the next letter will appear.

Switching Task: This test is a test of attention switching requiring spatial processing and working memory. In this task, subjects must alternate between two tasks presented simultaneously. The screen is divided such that the Mannequin Task is presented on the left half of the screen, and the Mathematical Processing Task is presented on the right half. At the bottom center of the screen is a bar, used to indicate which task subjects are to perform. The current task is indicated by the solid side of the bar. In the Mannequin task, a stick-like figure is presented holding a circle in one hand, and a square in the other. At the feet of the mannequin, either a circle or a square is shown in a box. The subjects task is to match the object in the box with the corresponding object in the mannequin's hands, and determine which hand the mannequin is holding the object in. The objects will not always be placed in the same hand and the orientation of the mannequin will change. The mannequin will be presented face forward, upright and upside down, and face backward, upright and upside down.

In Mathematical Processing Task, subjects must solve a number of simple addition and subtraction problems to determine whether the correct answer is less or greater than 5. The problems appear one at a time on the screen. Each problem requires two operations (addition and/or subtraction).

Reaction Time Task (Time Uncertainty Block): This test is similar to the Procedural Memory--Procedural Reaction Time basic block with additional difficulties: Numbers appear on the left or right side of the screen and subjects must respond with the corresponding hand. In addition, numbers are presented at irregular intervals.

Continuous Recognition Task: This test is a test of working or short term memory. Subjects are presented with a series of two numbers, one appearing above the other. Their task is to memorize the bottom number, and decide whether the top number is the same as the bottom number that was memorized one screen earlier.

Two-Column Addition: This test is a subject-paced mental arithmetic task. Five two-digit numbers are presented simultaneously in column format in the center of the screen. The subject determines their sum as rapidly as possible and enters it from the keyboard, beginning with the hundreds digit. The column of digits disappears with the first key entry, and no aids for the carry operation are allowed.

Digit Recall: This test is a test of short-term memory capacity. Nine random digits are displayed simultaneously in row across the center of the screen for one second. After a three second blank retention interval eight of the original nine digits are re-displayed in a different random order and the subject enters the missing digit. A given digit may appear no more than twice on each trial, although subjects are not informed of nor usually aware of this constraint.

Probed Force Memory Recall: This test is a test of delayed memory recall. Subjects are presented with four word pairs. Two of the pairs have a high degree of relatedness and two have a

low degree of relatedness. After the word pairs are memorized subject complete a 10 min performance vigilance test and then are tested for recall. Subjects are presented with the first of each word pair in a different order than originally presented and asked to give the matching word.

Wilkinson Four Choice Serial Reaction Time: This test is a simple test of continuous reaction time. The subject is presented with a box on the computer screen made up of four quadrants. A single quadrant is illuminated randomly and the subject is to press the corresponding button on the computer keyboard as quickly as possible, thereby initiating the next trial.

Modified Psychomotor Vigilance Test: This test is a test of simple reaction time with a time delay between stimulus presentation. Subjects are required to respond to a circle appearing in the middle of the computer screen as quickly as possible by pressing the space bar on the computer keyboard. Stimuli appear randomly every 3 to 17 s. The task takes 10 min to complete.

Alertness Assessment

Modified Psychomotor Vigilance Test: This test is a test of simple reaction time with a time delay between stimulus presentation. Subjects are required to respond to a circle appearing in the middle of the computer screen as quickly as possible by pressing the space bar on the computer keyboard. Stimuli appear randomly every 3 to 17 s. The task takes 10 min to complete.

Maintenance of Wakefulness Test: This test is a test of the subjects ability to maintain wakefulness. Subjects are placed in a position conducive to sleep (reclined in a lazy boy chair), told to keep their eyes open, and are informed that their task is to remain awake (Mitler et al., 1982)

Spectral Analysis of the EEG: This test is a test of subjects brain activity. Subjects are required to sit still for one minute (eyes closed) while their brain activity is monitored. Higher levels of Delta and Theta EEG activity are typically associated with sleepiness or the transition to sleep and higher levels of Alpha and Beta EEG with wakefulness (e.g., Wright et al., 1995).

Stanford Sleepiness Scale: This test assesses subjective sleepiness. Seven statements are displayed regarding subjective fatigue. Subjects pick the one best describing the state they are in (Hoddes et al., 1973).

Bibliography (Prior Publication of Results)

Badia, P., Wright, K. P., Jr., Myers, B. L., Plenzler, S., & Hakel, M. (1997). Effect of oral contraceptives and menstrual cycle phase on nighttime melatonin, body temperature and alertness levels in sleep deprived humans. Sleep Research, 26, 699.

Wright, K. P., Jr., Badia, P., Myers, B. L., Plenzler, S., & Drake, C. (1997). Caffeine and bright light effects on nighttime melatonin and body temperature in women. Sleep Research, 26, 636.

Wright, K. P., Jr., Badia, P., Plenzler, S., Myers, B. L., & Drake, C. (1997). Enhancement of nighttime alertness and performance in women with bright light and caffeine during 48 hr of sleep deprivation. Sleep Research, 26, 635.

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FIGURE CAPTIONS

General Figure Legend

DLP = Dim Light Placebo

DLC = Dim Light Caffeine

BLP = Bright Light Placebo

BLC = Bright Light Caffeine

DLP-FOL = Dim Light Placebo-Follicular Phase

DLP-LUT = Dim Light Placebo-Luteal Phase

DLP-OC = Dim Light Placebo-Oral Contraceptive

DLC-LUT = Dim Light Caffeine-Luteal Phase

DLC-OC = Dim Light Caffeine-Oral Contraceptive

BLP-LUT = Bright Light Placebo-Luteal Phase

BLP-OC = Bright Light Caffeine-Oral Contraceptive

BLC-LUT = Bright Light Placebo-Luteal Phase

BLC-OC = Bright Light Caffeine-Oral Contraceptive

For Performance Tasks:

P = last practice trial prior to treatment onset Friday (1700 hr);

1) the higher the Throughput scores = the better the performance,
2) the lower the Control Losses or reaction time = the better the performance.

For Alertness Tests:

1) the longer the Latency to Sleep on the MWT = the more alert,
2) the higher the Score on the SSS = the more sleepy.

Notes. Clock time on the abscissa represents the middle of each 3 hr testing block.

Effects of Sleep Deprivation, Menstrual Cycle Phase (Follicular, Luteal), and Oral Contraceptive Use

Graphs showing the effects of menstrual cycle phase (Follicular vs. Luteal) and Oral Contraceptive use on women's responses to sleep deprivation and on circadian rhythms. Data are presented for women tested under Dim Light Placebo conditions.

Figure Legend

DLP-FOL = Dim Light Placebo-Follicular Phase

DLP-LUT = Dim Light Placebo-Luteal Phase

DLP-OC = Dim Light Placebo-Oral Contraceptive

For Performance Tasks:

P = last practice trial prior to treatment onset Friday (1700 hr);

1) the higher the Throughput scores = the better the performance,
2) the lower the Control Losses = the better the performance.

For Alertness Tests:

1) the longer the Latency to Sleep on the MWT = the more alert,
2) the higher the Score on the SSS = the more sleepy.

Figure 1. **A)** Latency to sleep on the Maintenance of Wakefulness Test, Night 1 and **B)** Subjective sleepiness on the Stanford Sleepiness Scale. Night 1.

Figure 2. Night 1 performance on the **A)** Switching Task - Math Throughput, **B)** Two Column Addition Task - Throughput, **C)** Digit Recall Task - Throughput., **D)** Reaction Time Task - Throughput, **E)** Dual Task - Throughput, **F)** Continuous Recognition Task - Throughput, **G)** Probed Forced Memory Recall Task - Number of Words Correct, **H)** Dual Task - Control Losses,

I) Switching Task - Mannequin Throughput, **J)** Psychomotor Vigilance Task - Average Reaction Time, and **K)** Wilkinson Four Choice Reaction Time Task - Throughput.

Figure 3. Mood for the Profile of Mood States 6 sub-scales on Night 1. **A)** Tension/Anxiety Dynamic, **B)** Fatigue/Inertia Dynamic, **C)** Vigor/Activity Dynamic, **D)** Anger/Hostility Dynamic, **E)** Confusion/Bewilderment Dynamic, **F)** Depression/Dejection Dynamic.

Figure 4. Hourly salivary melatonin levels from 2000 to 1000 hr Night 1 **A)** Raw data, and **B)** Log transformation.

Figure 5. Hourly tympanic temperature from **A)** 2000 to 1000 hr Night 1, and **B)** 1000 Day 1 to 1000 Day 2.

Effects of Treatments (Caffeine, Bright Light)

Graphs showing the effects of sleep deprivation on women regardless of menstrual phase and oral contraceptive use.

Figure Legend

DLP = Dim Light Placebo
DLC = Dim Light Caffeine
BLP = Bright Light Placebo
BLC = Bright Light Caffeine

For Performance Tasks:

P = last practice trial prior to treatment onset Friday (1700 hr);

1) the higher the Throughput scores = the better the performance,
2) the lower the Control Losses = the better the performance.

For Alertness Tests:

1) the longer the Latency to Sleep on the MWT = the more alert,
2) the higher the Score on the SSS = the more sleepy.

Figure 6. **A)** Latency to sleep on the Maintenance of Wakefulness Test, and **B)** Subjective sleepiness on the Stanford Sleepiness Scale.

Figure 7. Performance on the **A)** Switching Task - Math Throughput, **B)** Two Column Addition Task - Throughput, **C)** Digit Recall Task - Throughput., **D)** Reaction Time Task - Throughput, **E)** Dual Task - Throughput, **F)** Continuous Recognition Task - Throughput, **G)** Probed Forced Memory Recall Task - Number of Words Correct, **H)** Dual Task - Control Losses, **I)** Switching Task - Mannequin Throughput, **J)** Psychomotor Vigilance Task - Average Reaction Time, and **K)** Wilkinson Four Choice Reaction Time Task - Throughput.

Figure 8. Mood for the Profile of Mood States 6 sub-scales. **A)** Tension/Anxiety Dynamic, **B)** Fatigue/Inertia Dynamic, **C)** Vigor/Activity Dynamic, **D)** Anger/Hostility Dynamic, **E)** Confusion/Bewilderment Dynamic, **F)** Depression/Dejection Dynamic.

Figure 9. **A)** Positive and **B)** Negative Affect for the Positive Affect Negative Affect Scale.

Figure 10. Hourly salivary melatonin levels 2000 to 1000 hr raw data **A)** Night 1 **B)** Night 2.

Figure 11. Hourly salivary melatonin levels from 2000 to 1000 hr, Log transformed data **A)** Night 1, and **B)** Night 2.

Figure 12. Hourly salivary melatonin levels from 2000 to 1000 hr. Night 1 for **A)** Luteal conditions, and **B)** Oral Contraceptive conditions.

Figure 13. Hourly tympanic temperature from 2000 to 1000 hr **A)** Night 1, and **B)** Night 2.

Figure 14. Hourly tympanic temperature from 2000 to 1000 hr for Night 1 **A)** Luteal conditions, and **B)** Oral Contraceptive conditions.

Figure 15. Tympanic temperature every 30 min for **A)** DLP conditions, **B)** BLP conditions, **C)** DLC conditions, and D) BLC conditions.

Influence of Oral Contraceptive Use concerning Effect s of Treatments

Graphs showing whether oral contraceptive use influences the effectiveness of the caffeine and bright light treatments to modify alertness, performance, and circadian rhythms in sleep deprived women.

Figure Legend

DLC-LUT = Dim Light Caffeine-Luteal Phase
DLC-OC = Dim Light Caffeine-Oral Contraceptive
BLP-LUT = Bright Light Placebo-Luteal Phase
BLP-OC = Bright Light Caffeine-Oral Contraceptive
BLC-LUT = Bright Light Placebo-Luteal Phase
BLC-OC = Bright Light Caffeine-Oral Contraceptive

For Performance Tasks:

P = last practice trial prior to treatment onset Friday (1700 hr);

1) the higher the Throughput scores = the better the performance,
2) the lower the Control Losses = the better the performance.

For Alertness Tests:

1) the longer the Latency to Sleep on the MWT = the more alert,
2) the higher the Score on the SSS = the more sleepy.

Figure 29. Mood for the Profile of Mood States **A)** Tension/Anxiety Dynamic - DLC-LUT, DLC-OC, **B)** Tension/Anxiety Dynamic - BLP-LUT, BLP-OC, **C)** Tension/Anxiety Dynamic - BLC-LUT, BLC-OC, **D)** Fatigue/Inertia Dynamic - DLC-LUT, DLC-OC, **E)** Fatigue/Inertia Dynamic - BLP-LUT, BLP-OC, **F)** Fatigue/Inertia Dynamic - BLC-LUT, BLC-OC, **G)** Vigor/Activity Dynamic - DLC-LUT, DLC-OC, **H)** Vigor/Activity Dynamic - BLP-LUT, BLP-OC, **I)** Vigor/Activity Dynamic - BLC-LUT, BLC-OC, **J)** Anger/Hostility Dynamic - DLC-LUT, DLC-OC, **K)** Anger/Hostility Dynamic - BLP-LUT, BLP-OC, **L)** Anger/Hostility Dynamic - BLC-LUT, BLC-OC, **M)** Confusion/Bewilderment Dynamic - DLC-LUT, DLC-OC, **N)** Confusion/Bewilderment Dynamic - BLP-LUT, BLP-OC, **O)** Confusion/Bewilderment Dynamic - BLC-LUT, BLC-OC, **P)** Depression/Dejection Dynamic - DLC-LUT, DLC-OC, **Q)** Depression/Dejection Dynamic - BLP-LUT, BLP-OC, and **R)** Depression/Dejection Dynamic - BLC-LUT, BLC-OC.

Figure 30. Hourly salivary melatonin levels from 2000 to 1000 hr. Night 1.

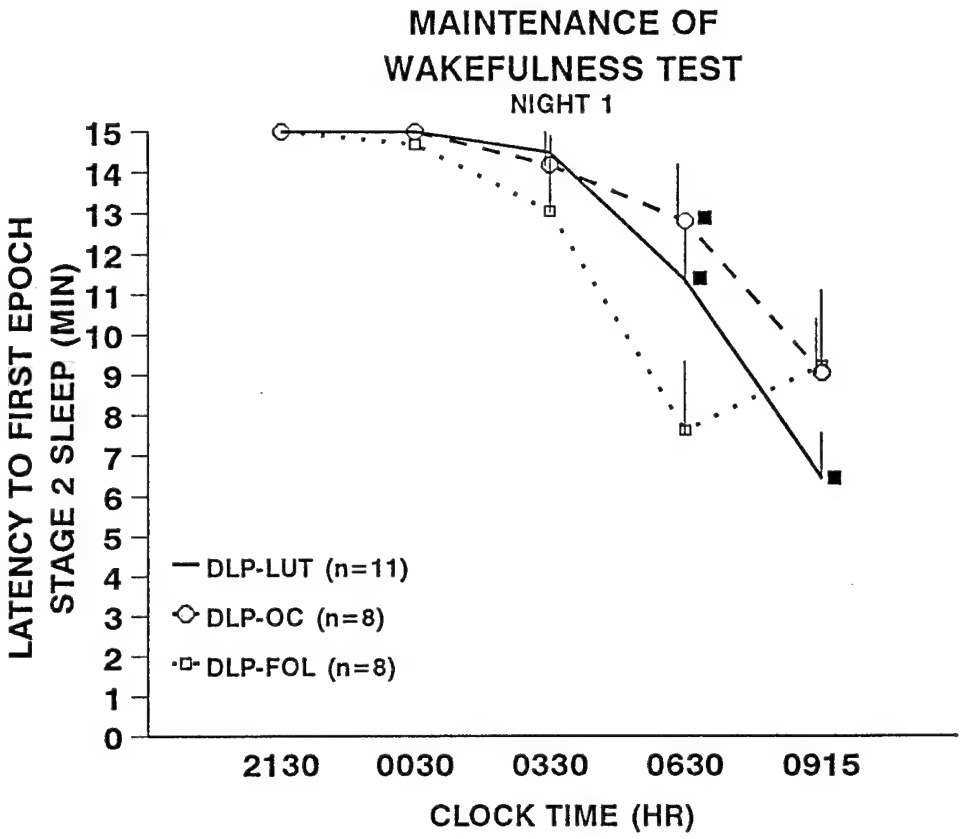
Figure 31. Log transformation of hourly salivary melatonin levels from 2000 to 1000 hr. Night 1.

Figure 32. Hourly tympanic temperature from 2000 to 1000 hr Night 1.

Figure 33. Hourly tympanic temperature from 1000 Day 1 to 1000 Day 2.

Figure 1

A


MAINTENANCE OF
WAKEFULNESS TEST
NIGHT 1
LATENCY TO FIRST EPOCH
STAGE 2 SLEEP (MIN)
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
2130
0030
0330
0630
0915
CLOCK TIME (HR)

B

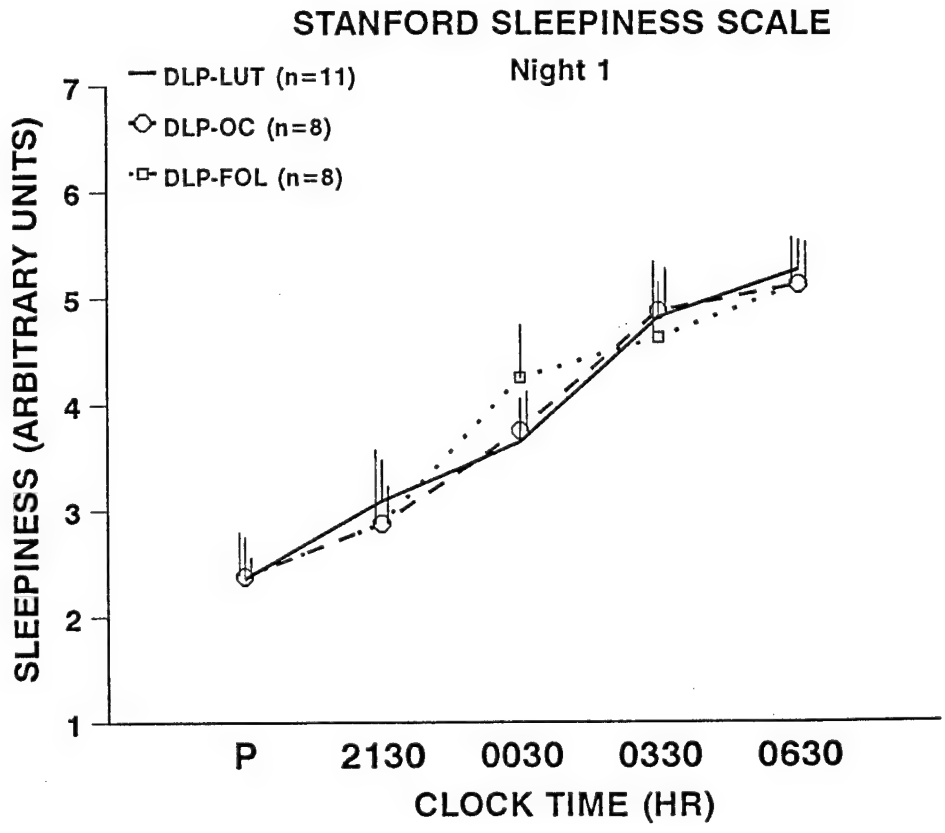
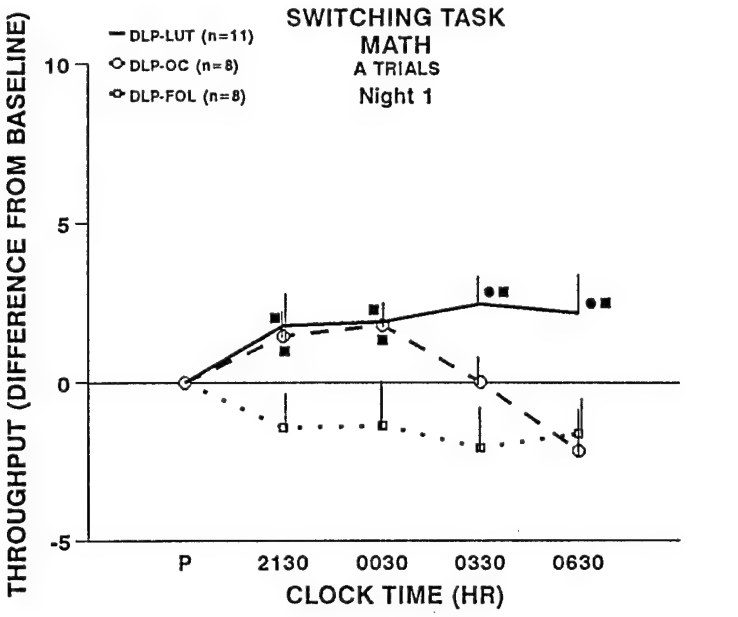
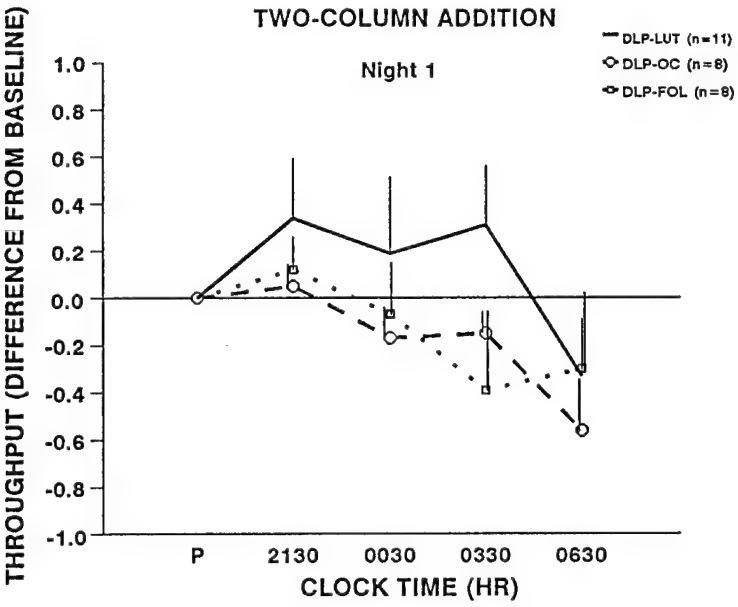

STANFORD SLEEPINESS SCALE
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
SLEEPINESS (ARBITRARY UNITS)
7
6
5
4
3
2
1
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 2

A


SWITCHING TASK
MATH
A TRIALS
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

B


TWO-COLUMN ADDITION
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
P
2130
0030
0330
0630
CLOCK TIME (HR)

C

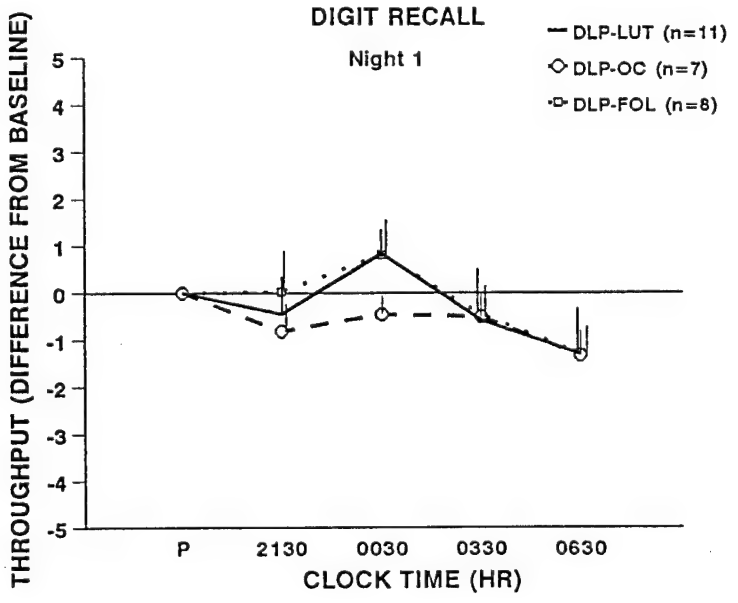
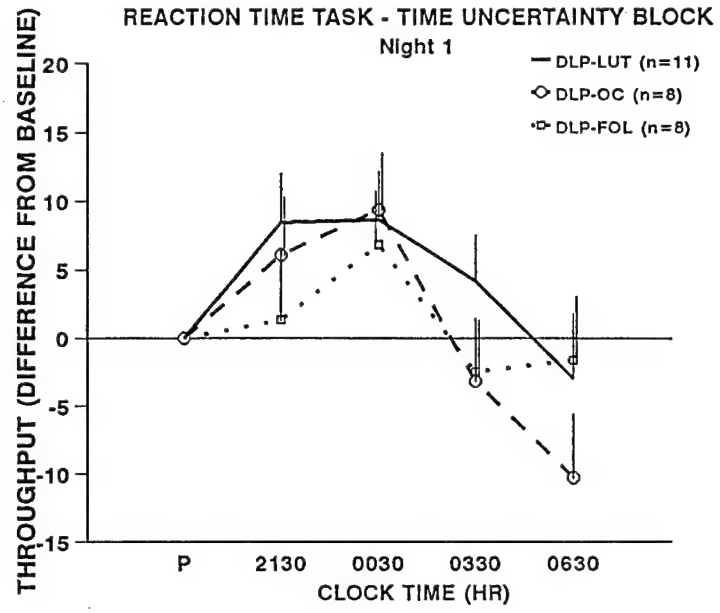
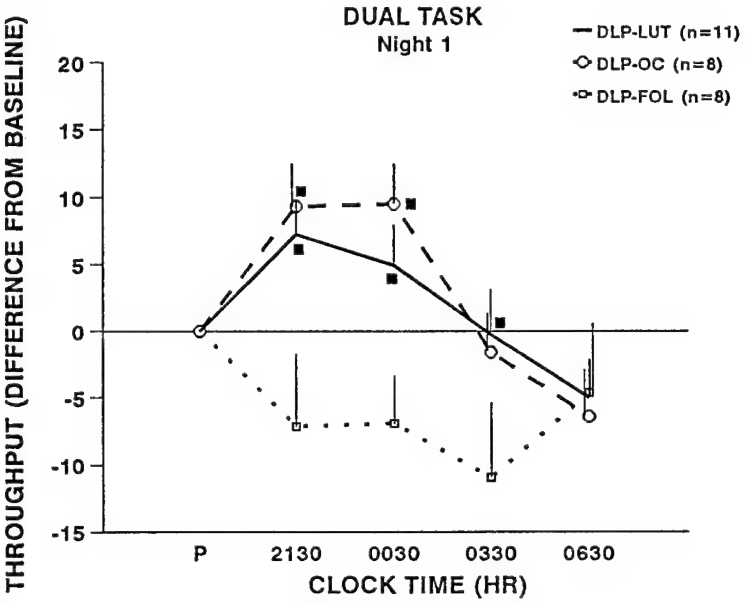

DIGIT RECALL
Night 1
DLP-LUT (n=11)
DLP-OC (n=7)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
5
4
3
2
1
0
-1
-2
-3
-4
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 2

D


REACTION TIME TASK - TIME UNCERTAINTY BLOCK
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)

E


DUAL TASK
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)

F

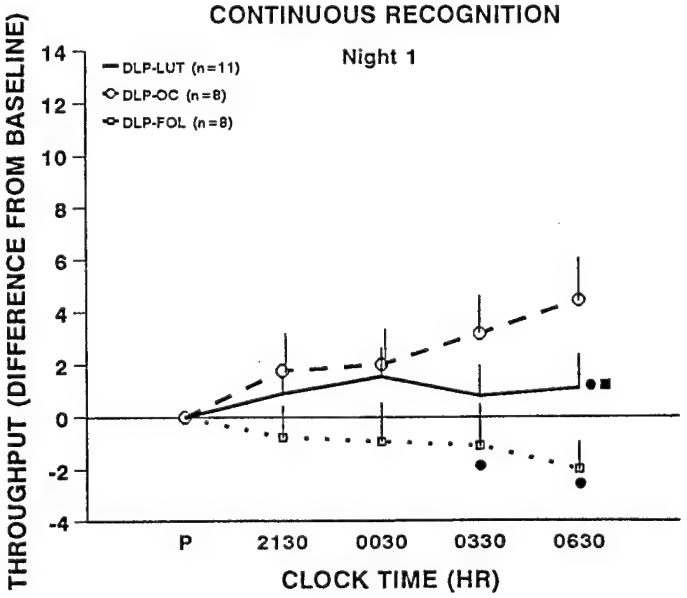
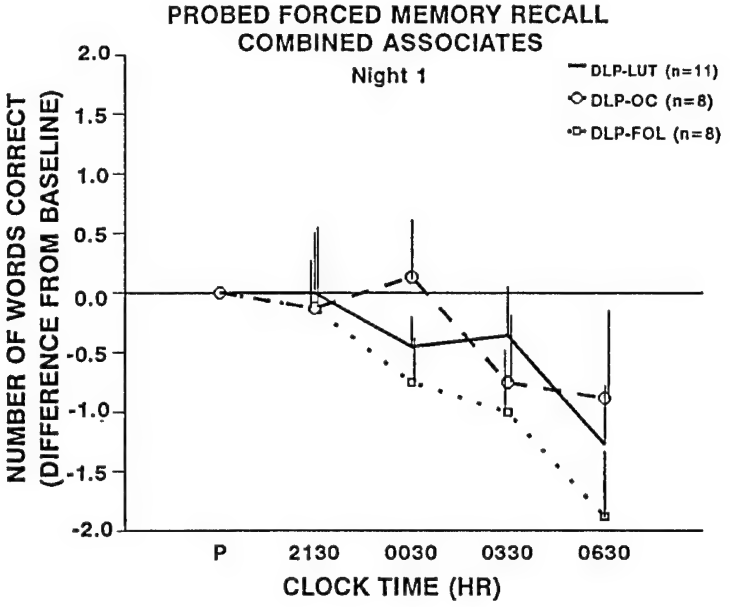
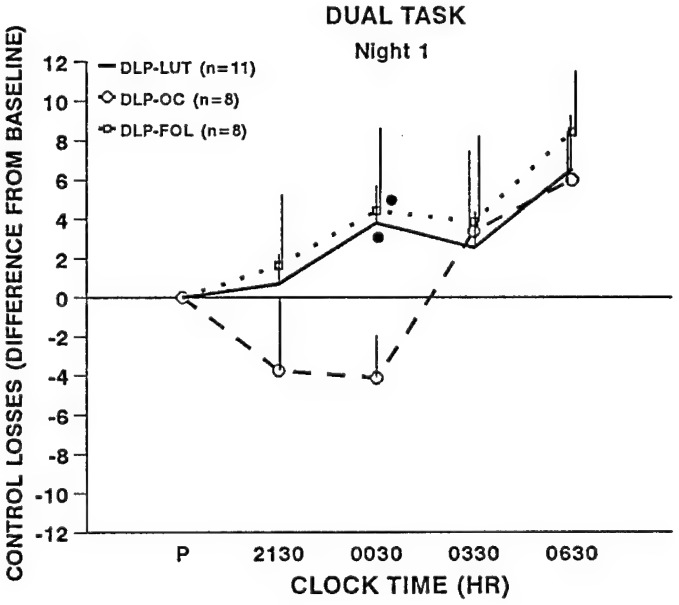

CONTINUOUS RECOGNITION
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
14
12
10
8
6
4
2
0
-2
-4
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 2

G


PROBED FORCED MEMORY RECALL
COMBINED ASSOCIATES
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
NUMBER OF WORDS CORRECT
(DIFFERENCE FROM BASELINE)
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
P
2130
0030
0330
0630
CLOCK TIME (HR)

H


DUAL TASK
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
CONTROL LOSSES (DIFFERENCE FROM BASELINE)
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
-12
P
2130
0030
0330
0630
CLOCK TIME (HR)

I

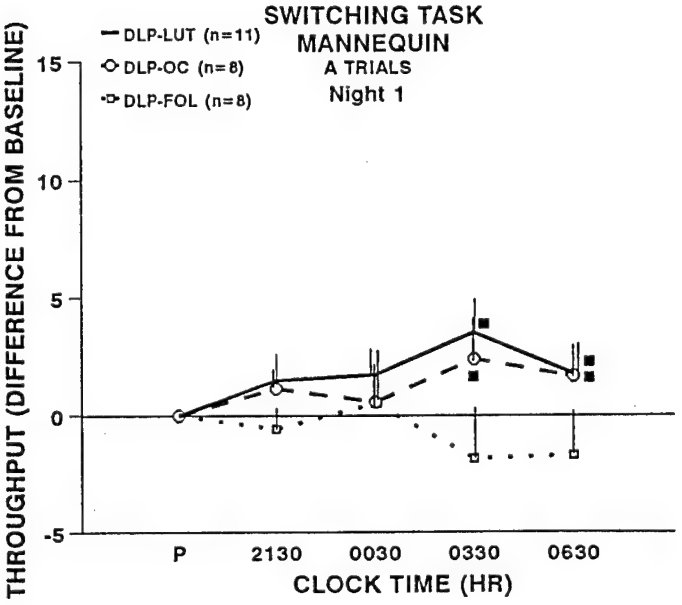
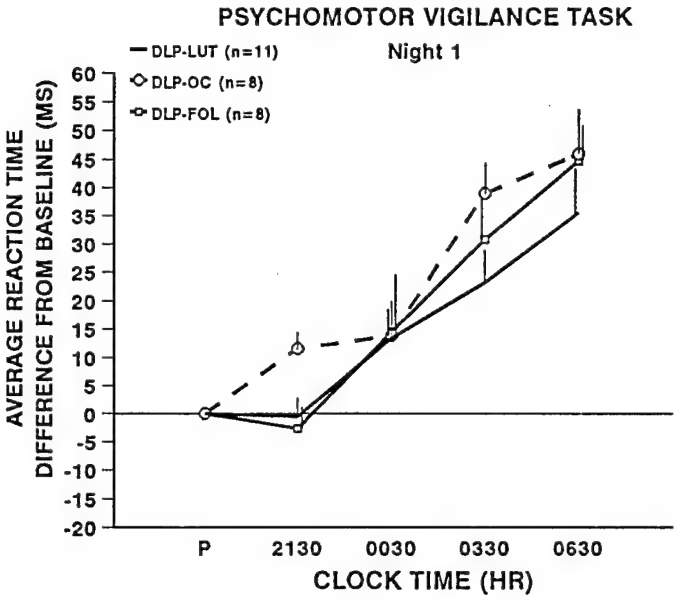
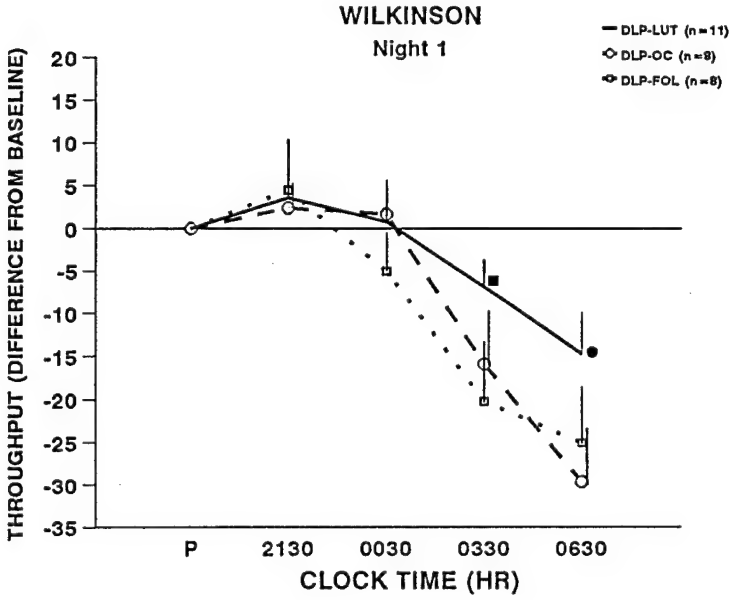

SWITCHING TASK
MANNEQUIN
A TRIALS
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
15
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 2

J


PSYCHOMOTOR VIGILANCE TASK
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
Night 1
AVERAGE REACTION TIME DIFFERENCE FROM BASELINE (MS)
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
P
2130
0030
0330
0630
CLOCK TIME (HR)

K


WILKINSON
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
P
2130
0030
0330
0630
CLOCK TIME (HR)

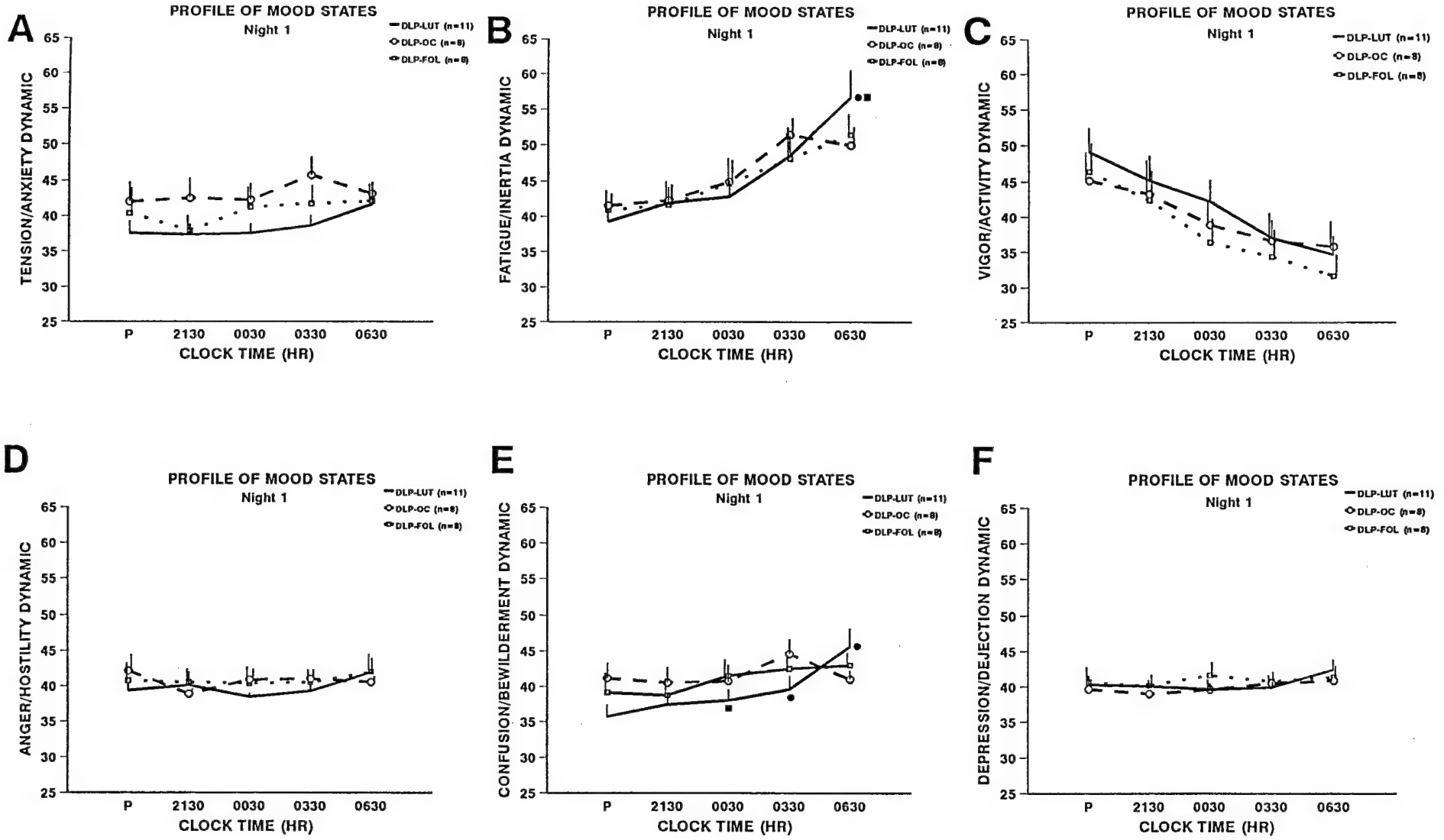
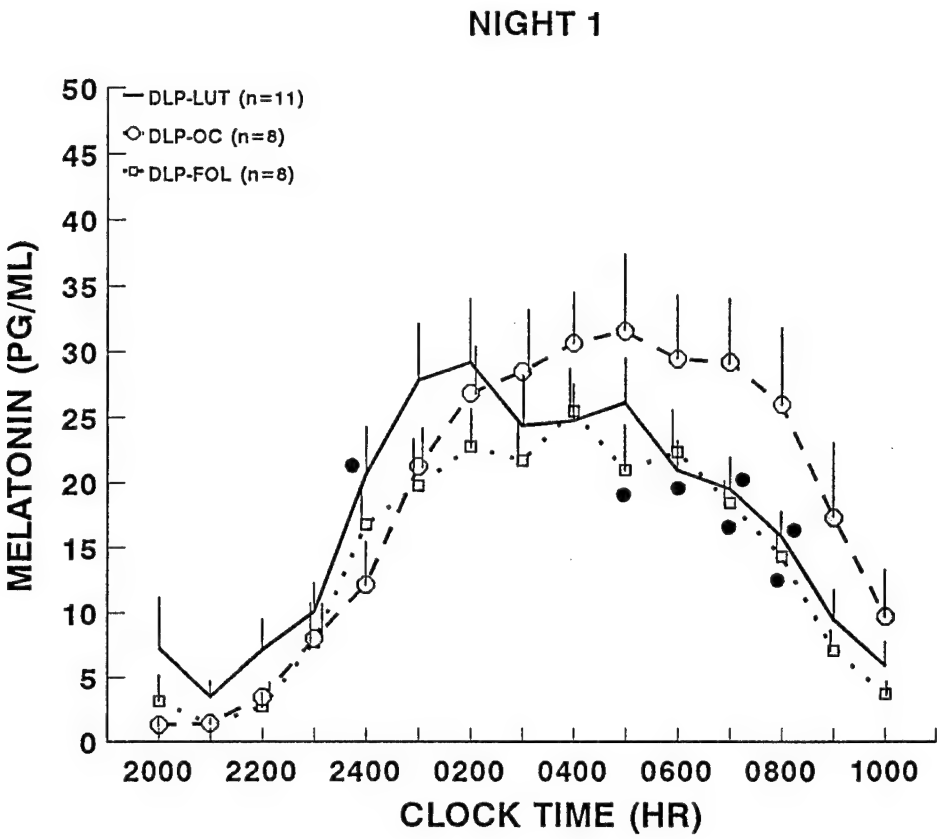

A
PROFILE OF MOOD STATES
Night 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
TENSION/ANXIETY DYNAMIC
CLOCK TIME (HR)
P
2130
0030
0330
0630
B
PROFILE OF MOOD STATES
Night 1
FATIGUE/INERTIA DYNAMIC
C
PROFILE OF MOOD STATES
Night 1
VIGOR/ACTIVITY DYNAMIC
D
PROFILE OF MOOD STATES
Night 1
ANGER/HOSTILITY DYNAMIC
E
PROFILE OF MOOD STATES
Night 1
CONFUSION/BEWILDERMENT DYNAMIC
F
PROFILE OF MOOD STATES
Night 1
DEPRESSION/DEJECTION DYNAMIC

Figure 3

Figure 4

A


NIGHT 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
MELATONIN (PG/ML)
50
45
40
35
30
25
20
15
10
5
0
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

B

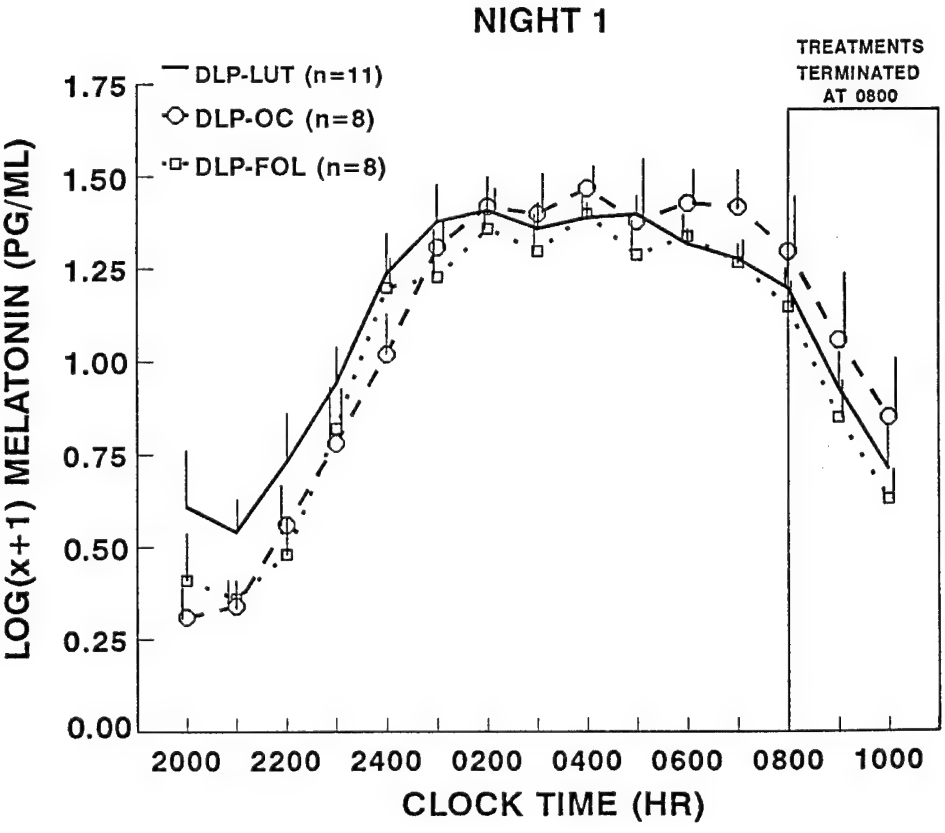
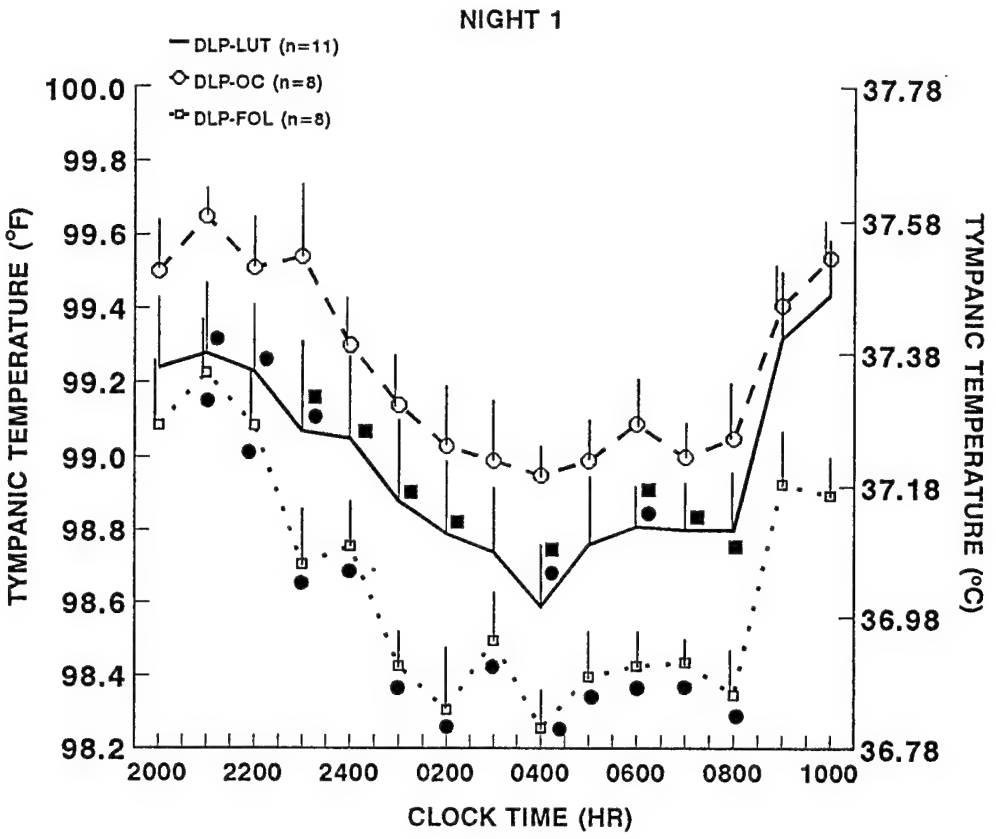

NIGHT 1
TREATMENTS TERMINATED AT 0800
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
LOG(x+1) MELATONIN (PG/ML)
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

Figure 5

A


NIGHT 1
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
TYMPANIC TEMPERATURE (°F)
TYMPANIC TEMPERATURE (°C)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
37.78
37.58
37.38
37.18
36.98
36.78
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

B

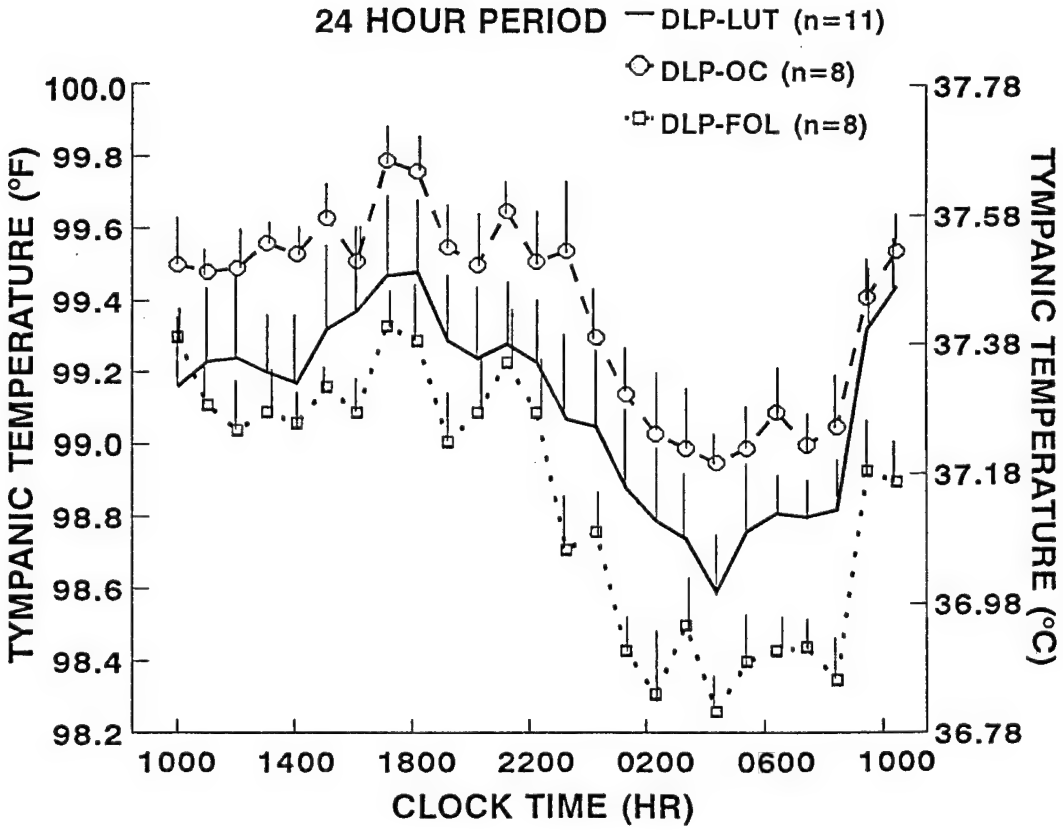
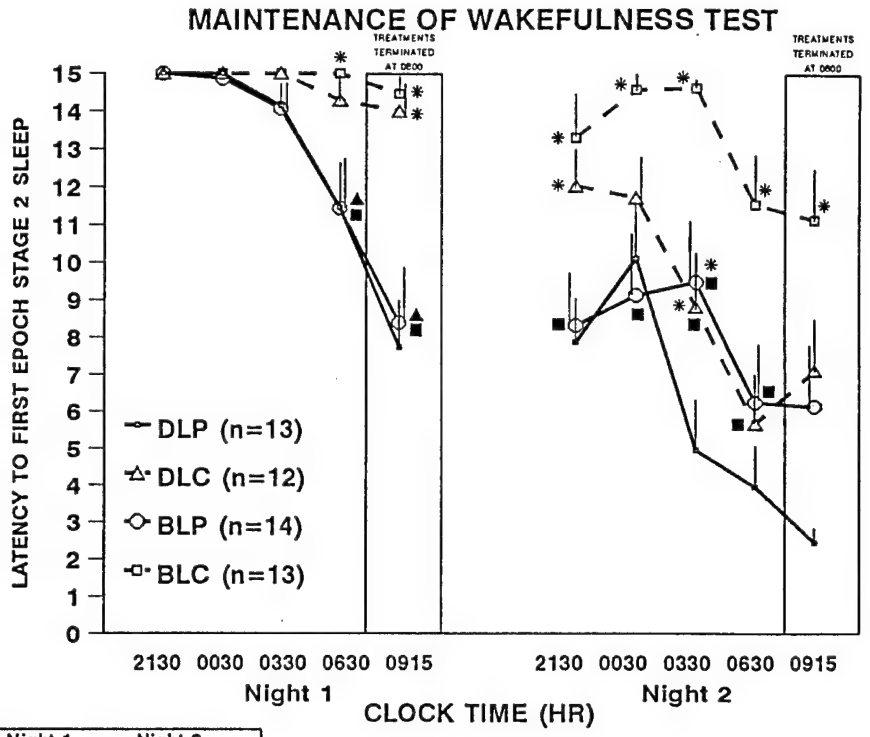

24 HOUR PERIOD
DLP-LUT (n=11)
DLP-OC (n=8)
DLP-FOL (n=8)
TYMPANIC TEMPERATURE (°F)
TYMPANIC TEMPERATURE (°C)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
37.78
37.58
37.38
37.18
36.98
36.78
1000
1400
1800
2200
0200
0600
1000
CLOCK TIME (HR)

Figure 6

A



	Night 1	Night 2	
DLP	13.90 (0.40)	6.73 (0.89)	n
DLC	14.82 (0.17)	9.57 (0.84) *	■ n
BLP	13.84 (0.45)	8.30 (1.31)	■ n
BLC	15.00 (0.00)	13.52 (0.57) *	

B

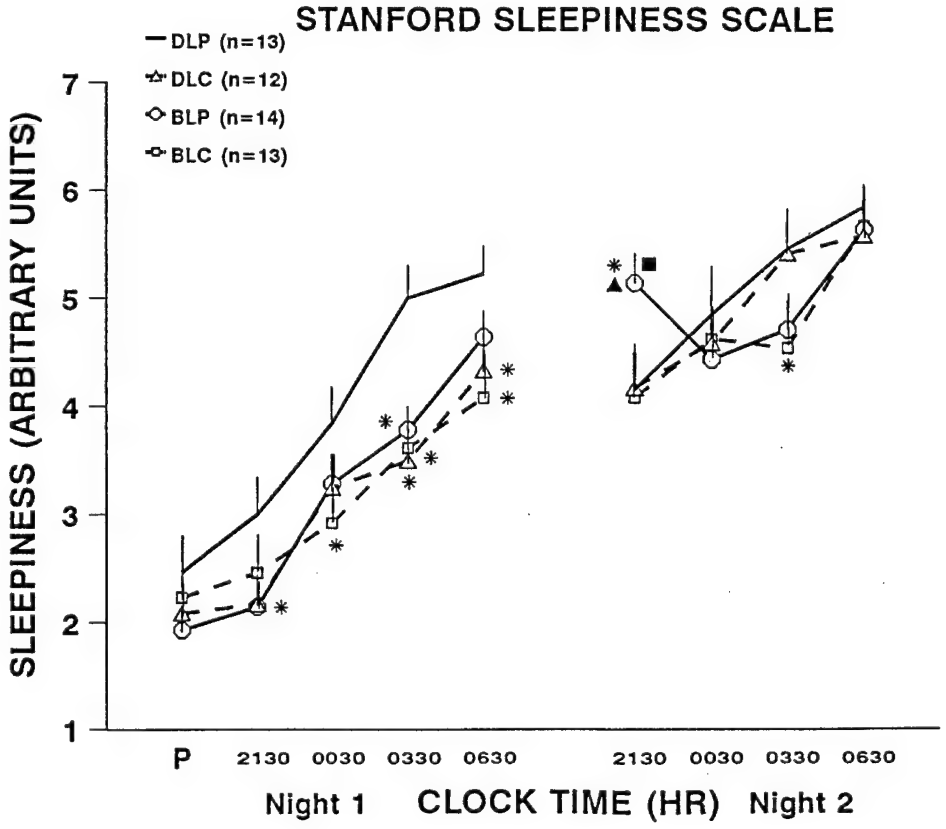
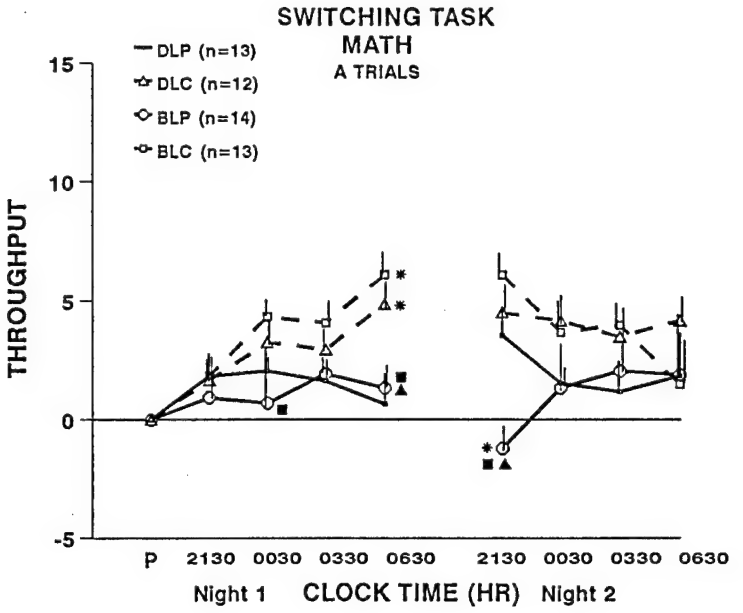
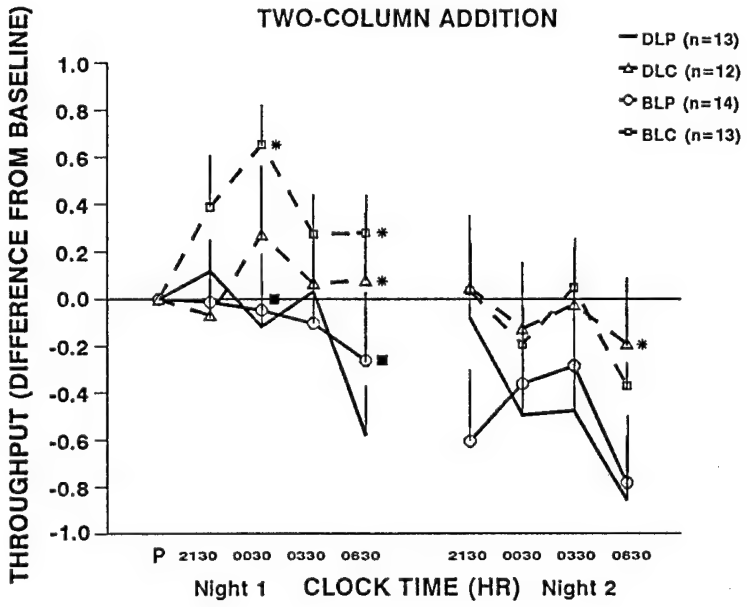


Figure 7

A


SWITCHING TASK
MATH
A TRIALS
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
THROUGHPUT
15
10
5
0
-5
P
2130
0030
0330
0630
2130
0030
0330
0630
Night 1
CLOCK TIME (HR)
Night 2

B


TWO-COLUMN ADDITION
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
THROUGHPUT (DIFFERENCE FROM BASELINE)
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
P
2130
0030
0330
0630
2130
0030
0330
0630
Night 1
CLOCK TIME (HR)
Night 2

C

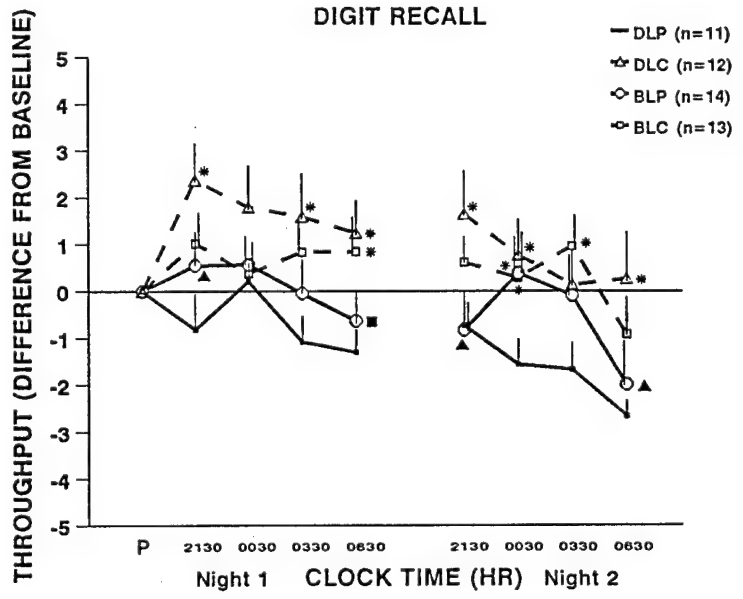
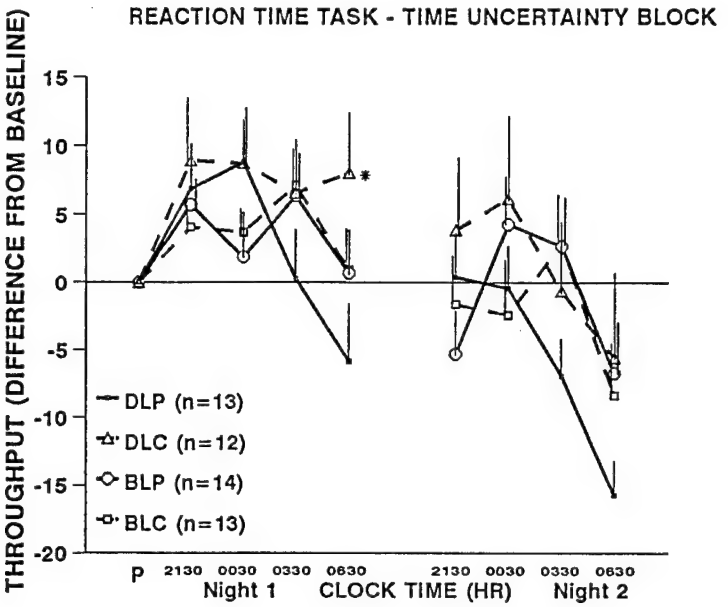
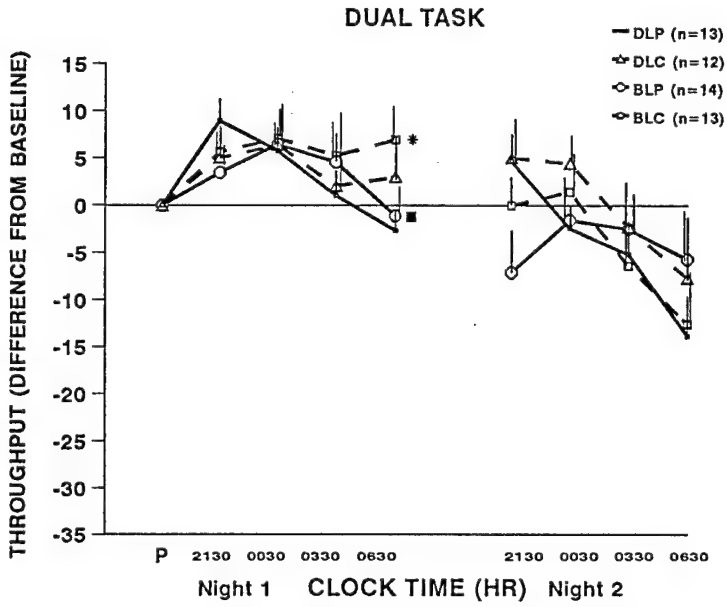

DIGIT RECALL
DLP (n=11)
DLC (n=12)
BLP (n=14)
BLC (n=13)
THROUGHPUT (DIFFERENCE FROM BASELINE)
5
4
3
2
1
0
-1
-2
-3
-4
-5
P
2130
0030
0330
0630
2130
0030
0330
0630
Night 1
CLOCK TIME (HR)
Night 2

Figure 7

D


REACTION TIME TASK - TIME UNCERTAINTY BLOCK
THROUGHPUT (DIFFERENCE FROM BASELINE)
15
10
5
0
-5
-10
-15
-20
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
P 2130 0030 0330 0630 2130 0030 0330 0630
Night 1 CLOCK TIME (HR) Night 2

E


DUAL TASK
THROUGHPUT (DIFFERENCE FROM BASELINE)
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
P 2130 0030 0330 0630 2130 0030 0330 0630
Night 1 CLOCK TIME (HR) Night 2

F

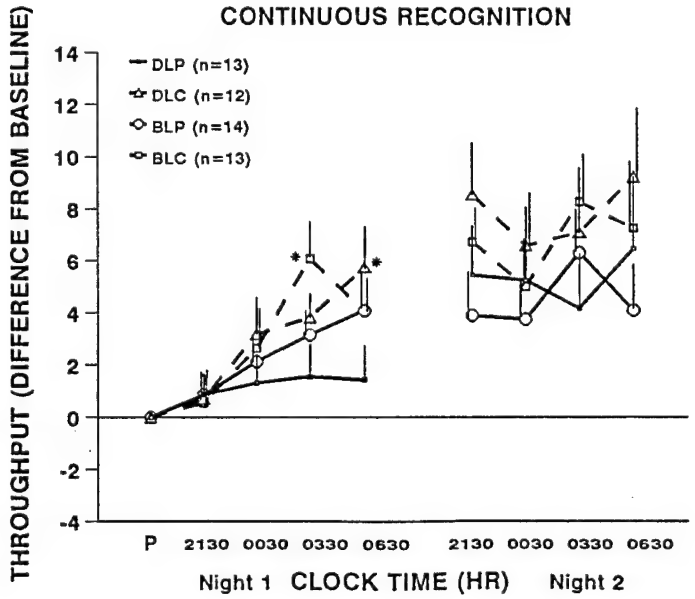
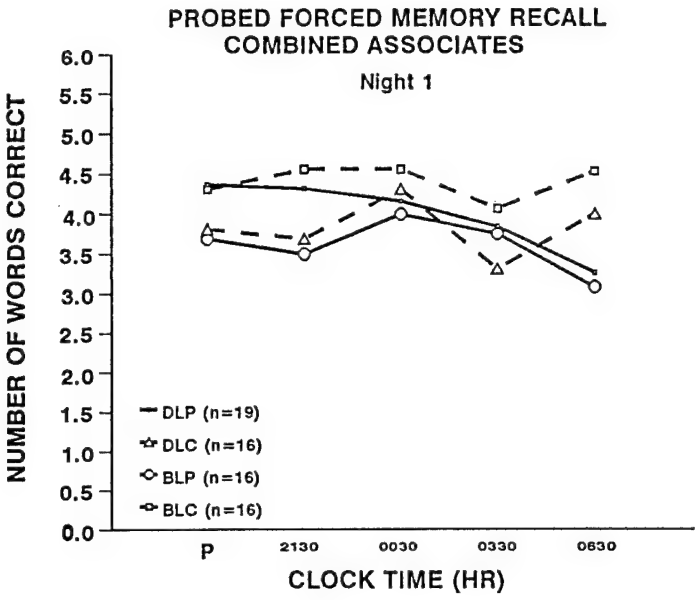
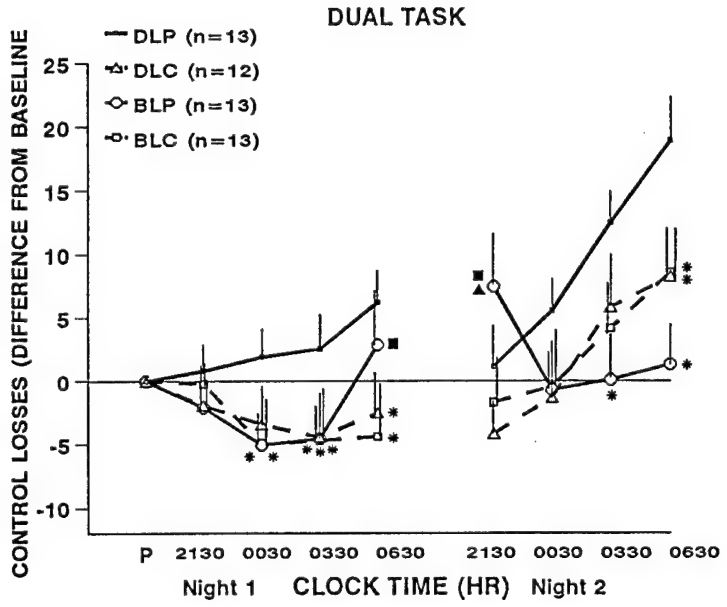

CONTINUOUS RECOGNITION
THROUGHPUT (DIFFERENCE FROM BASELINE)
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
14
12
10
8
6
4
2
0
-2
-4
P 2130 0030 0330 0630 2130 0030 0330 0630
Night 1 CLOCK TIME (HR) Night 2

Figure 7

G


PROBED FORCED MEMORY RECALL
COMBINED ASSOCIATES
Night 1
NUMBER OF WORDS CORRECT
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
DLP (n=19)
DLC (n=16)
BLP (n=16)
BLC (n=16)
P
2130
0030
0330
0630
CLOCK TIME (HR)

H


DUAL TASK
DLP (n=13)
DLC (n=12)
BLP (n=13)
BLC (n=13)
CONTROL LOSSES (DIFFERENCE FROM BASELINE
25
20
15
10
5
0
-5
-10
P
2130
0030
0330
0630
2130
0030
0330
0630
Night 1
CLOCK TIME (HR)
Night 2

I

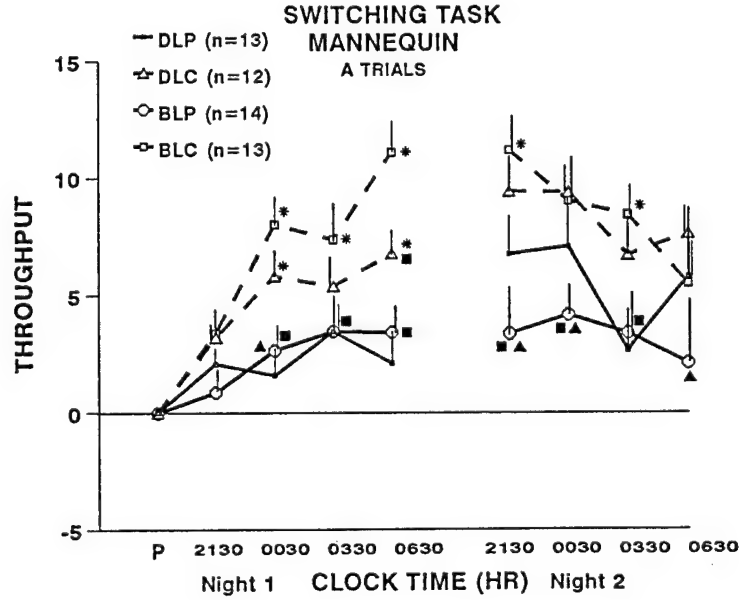
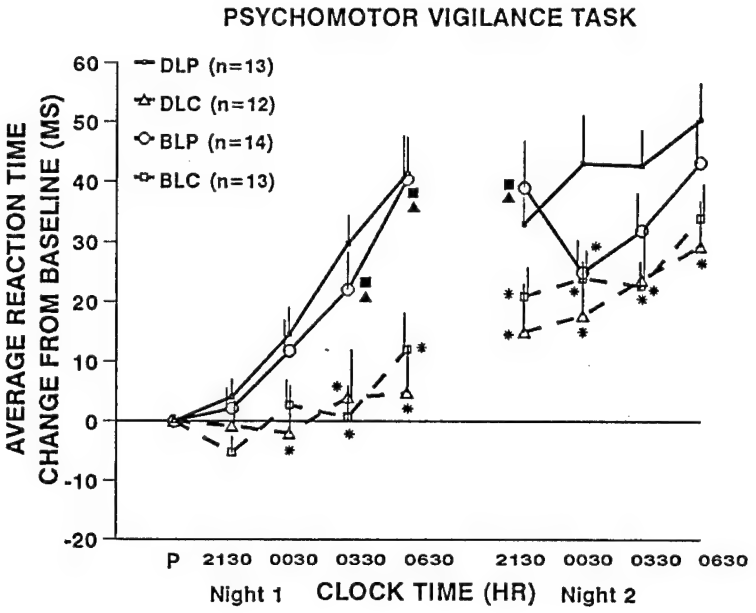
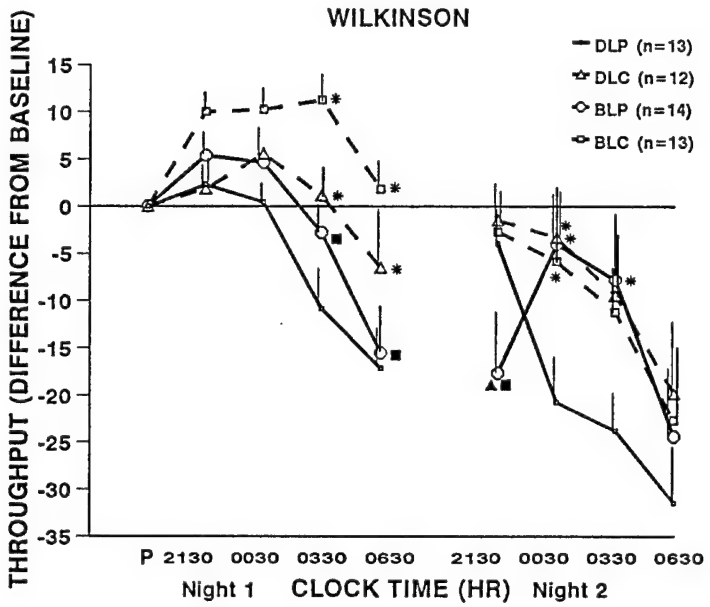

SWITCHING TASK
MANNEQUIN
A TRIALS
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
THROUGHPUT
15
10
5
0
-5
P
2130
0030
0330
0630
2130
0030
0330
0630
Night 1
CLOCK TIME (HR)
Night 2

Figure 7

J


PSYCHOMOTOR VIGILANCE TASK
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
AVERAGE REACTION TIME CHANGE FROM BASELINE (MS)
60
50
40
30
20
10
0
-10
-20
P 2130 0030 0330 0630 2130 0030 0330 0630
Night 1 CLOCK TIME (HR) Night 2

K


WILKINSON
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
THROUGHPUT (DIFFERENCE FROM BASELINE)
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
P 2130 0030 0330 0630 2130 0030 0330 0630
Night 1 CLOCK TIME (HR) Night 2

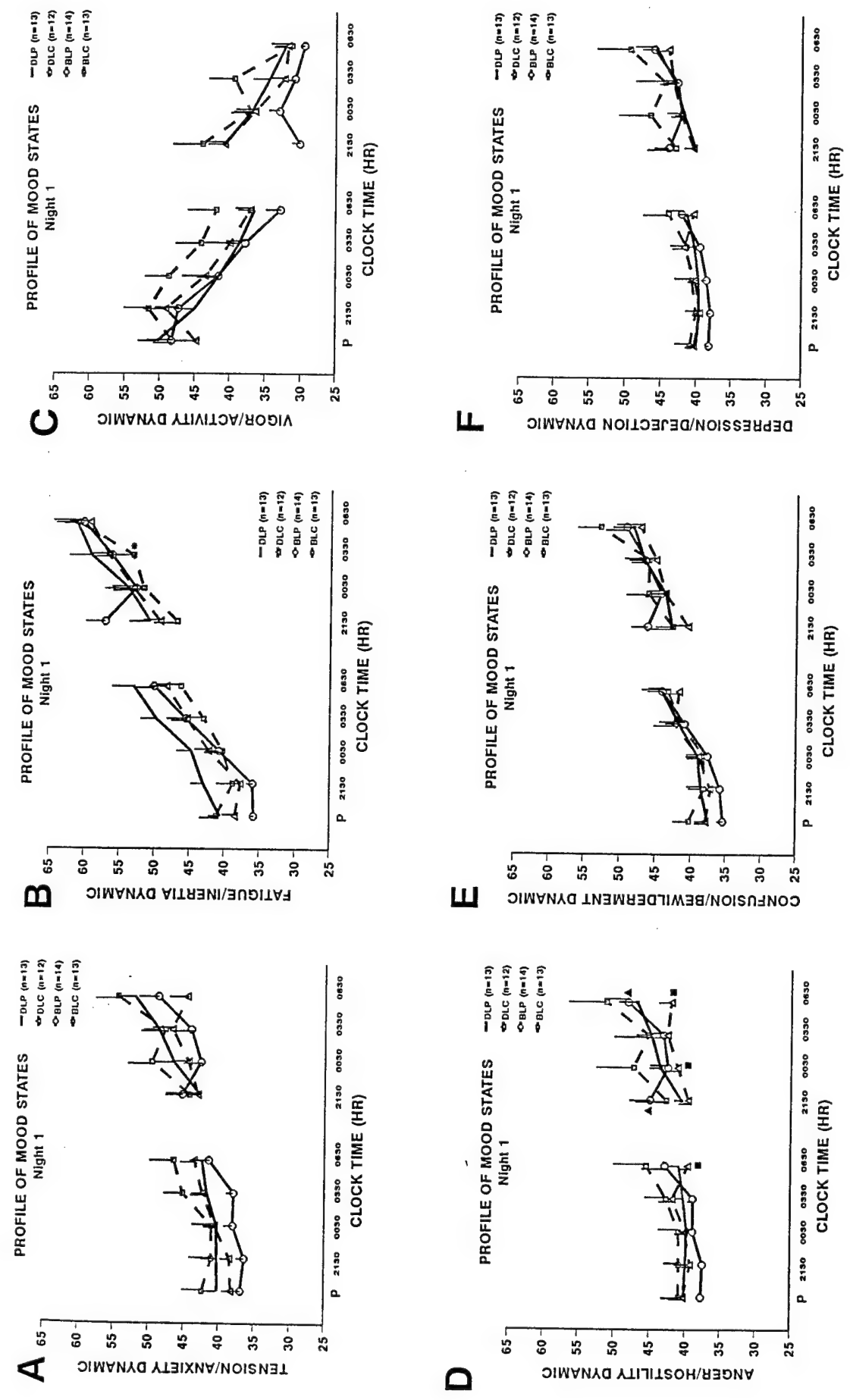
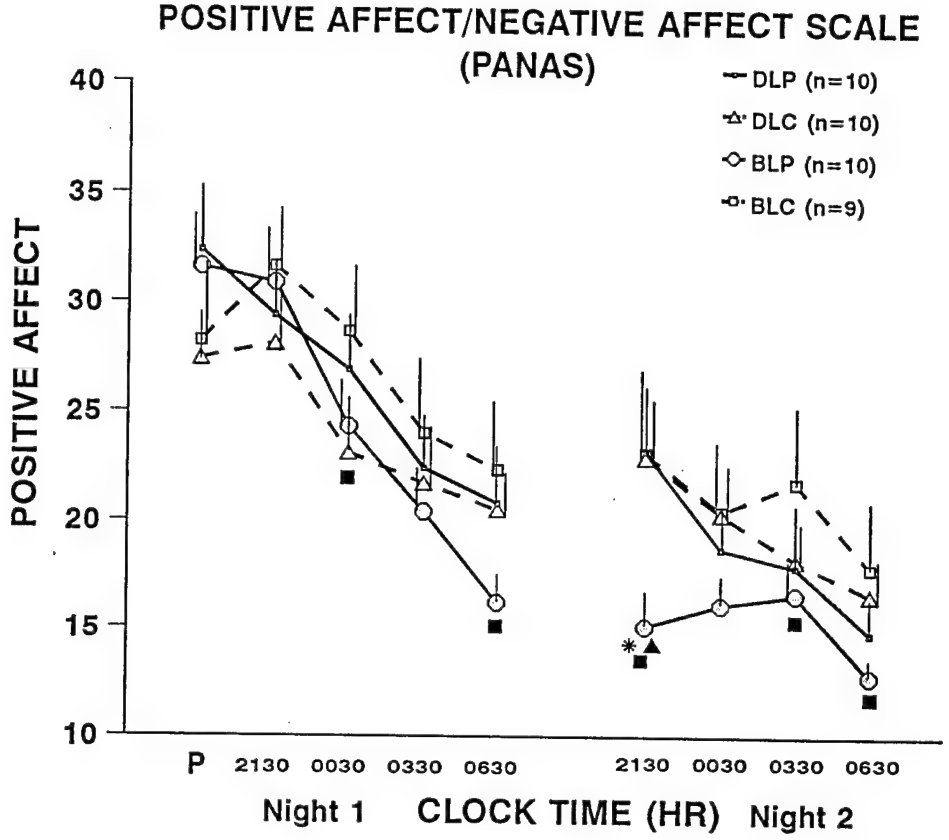

A
PROFILE OF MOOD STATES
Night 1
TENSION/ANXIETY DYNAMIC
CLOCK TIME (HR)
B
PROFILE OF MOOD STATES
Night 1
FATIGUE/INERTIA DYNAMIC
CLOCK TIME (HR)
C
PROFILE OF MOOD STATES
Night 1
VIGOR/ACTIVITY DYNAMIC
CLOCK TIME (HR)
D
PROFILE OF MOOD STATES
Night 1
ANGER/HOSTILITY DYNAMIC
CLOCK TIME (HR)
E
PROFILE OF MOOD STATES
Night 1
CONFUSION/BEWILDERMENT DYNAMIC
CLOCK TIME (HR)
F
PROFILE OF MOOD STATES
Night 1
DEPRESSION/DEJECTION DYNAMIC
CLOCK TIME (HR)
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)

Figure 8

Figure 9

A


POSITIVE AFFECT/NEGATIVE AFFECT SCALE
(PANAS)
DLP (n=10)
DLC (n=10)
BLP (n=10)
BLC (n=9)
POSITIVE AFFECT
40
35
30
25
20
15
10
P
2130
0030
0330
0630
2130
0030
0330
0630
Night 1
CLOCK TIME (HR)
Night 2

B

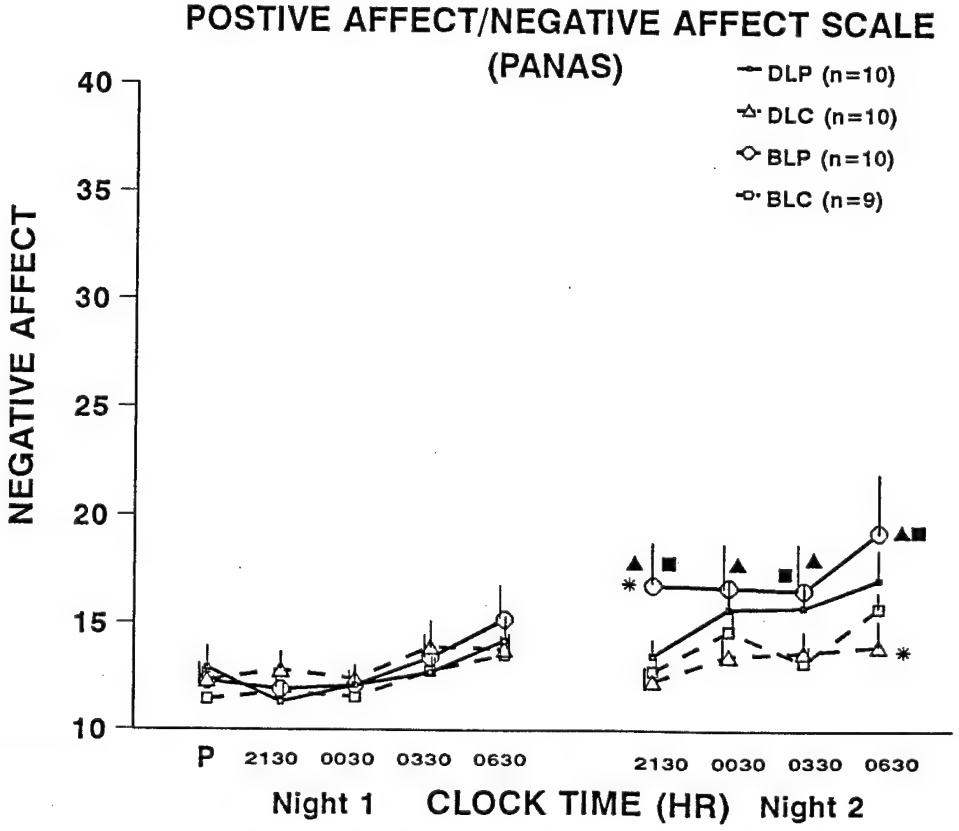
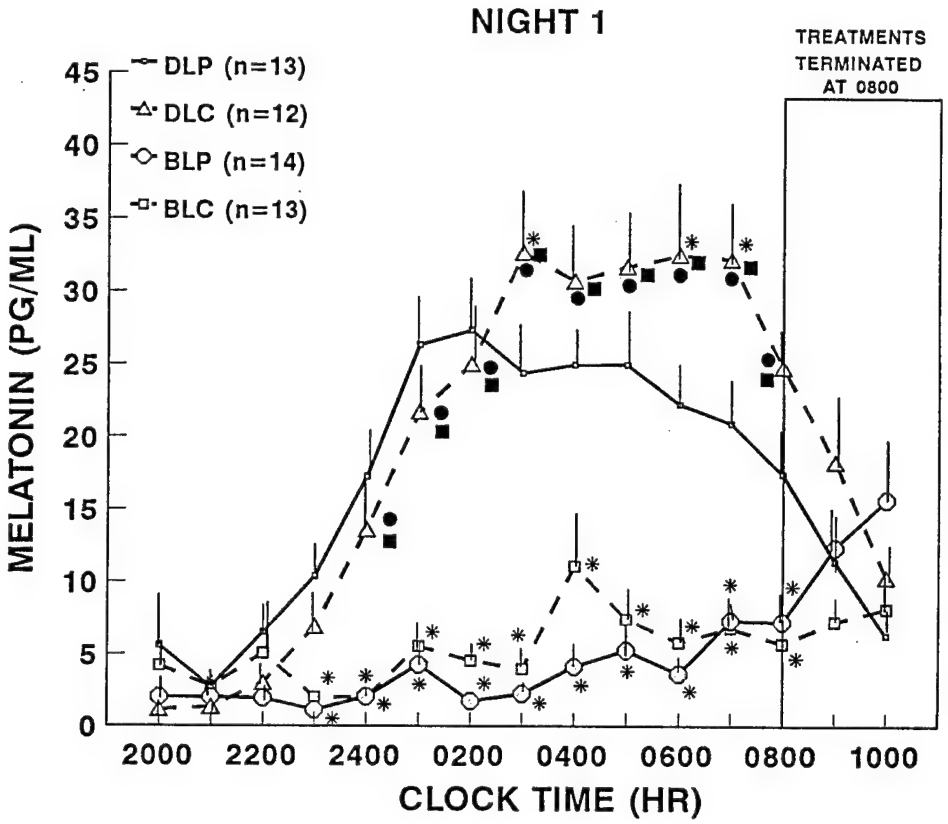

POSTIVE AFFECT/NEGATIVE AFFECT SCALE
(PANAS)
DLP (n=10)
DLC (n=10)
BLP (n=10)
BLC (n=9)
NEGATIVE AFFECT
40
35
30
25
20
15
10
P
2130
0030
0330
0630
2130
0030
0330
0630
Night 1
CLOCK TIME (HR)
Night 2

Figure 10 **A**


NIGHT 1
TREATMENTS TERMINATED AT 0800
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
MELATONIN (PG/ML)
0
5
10
15
20
25
30
35
40
45
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

B

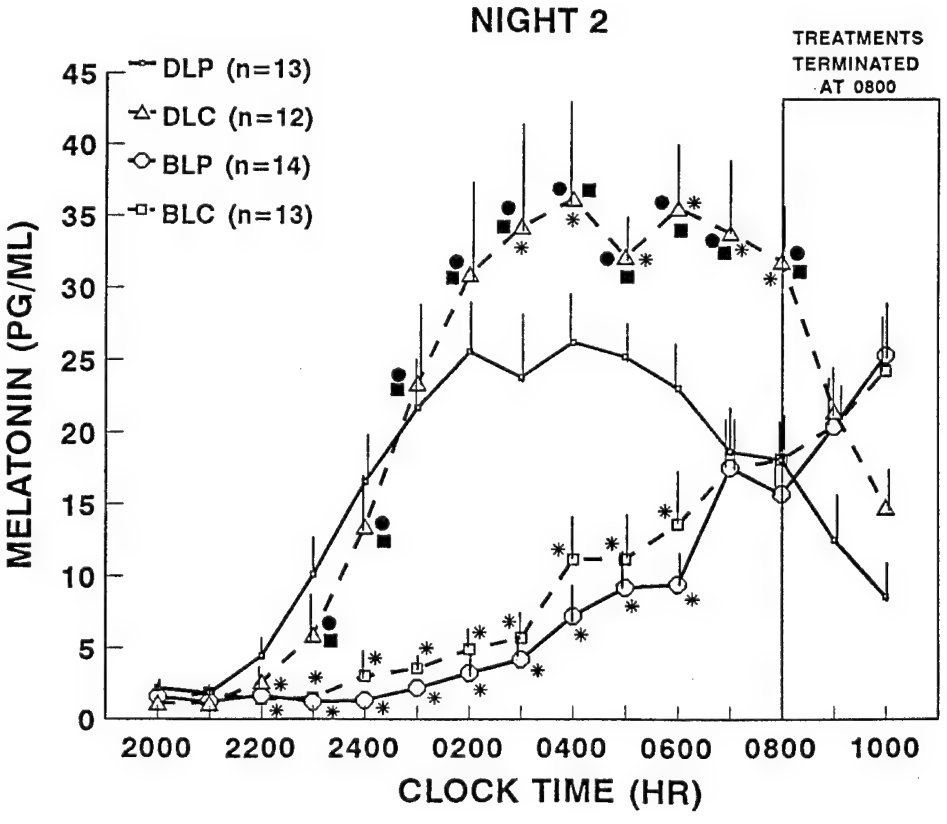
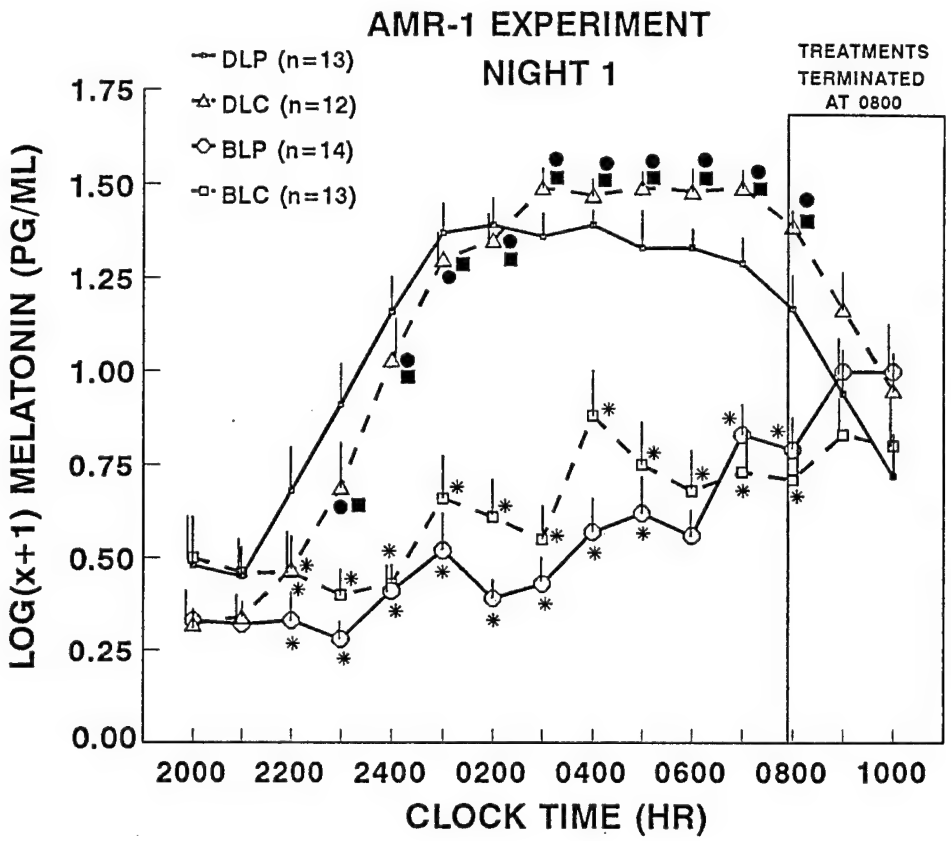
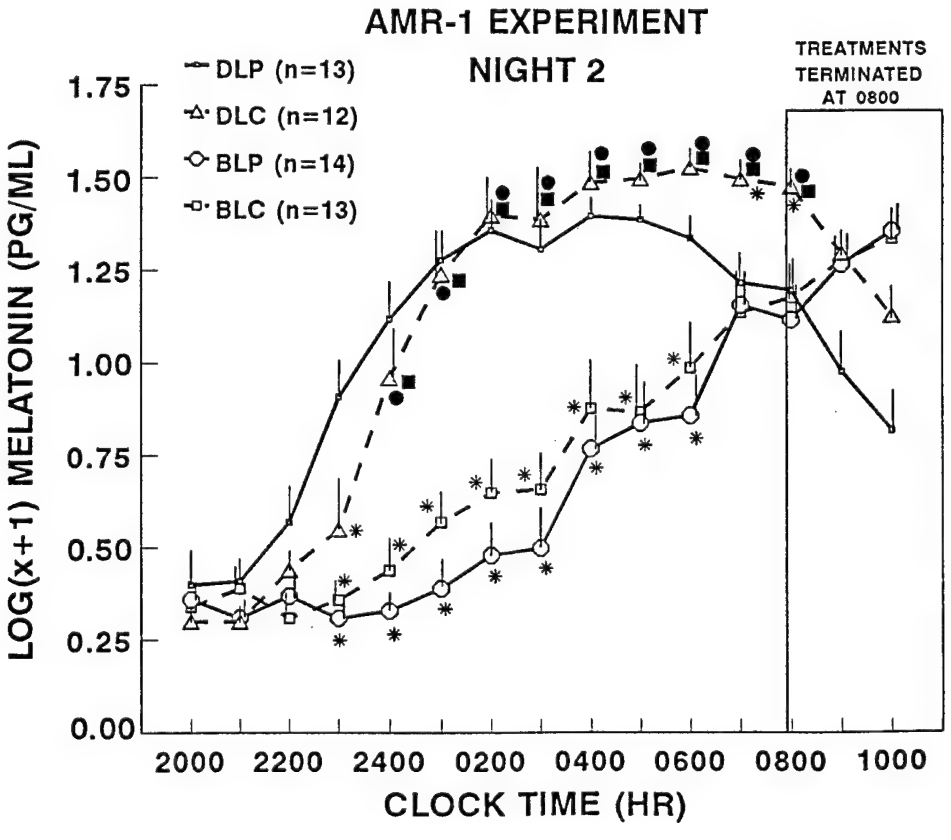

NIGHT 2
TREATMENTS TERMINATED AT 0800
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
MELATONIN (PG/ML)
0
5
10
15
20
25
30
35
40
45
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

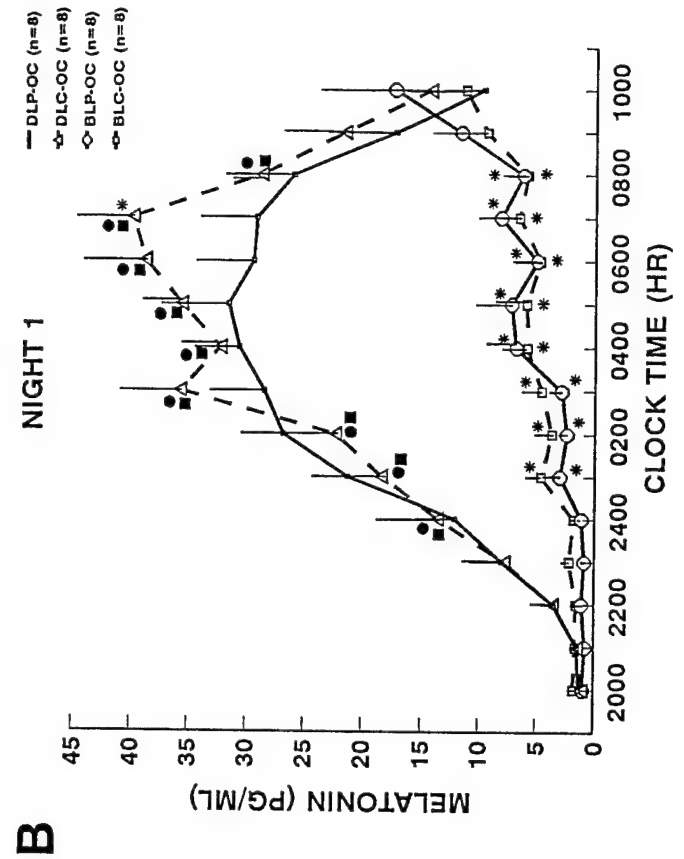
Figure 11

A


AMR-1 EXPERIMENT
NIGHT 1
TREATMENTS TERMINATED AT 0800
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
LOG(x+1) MELATONIN (PG/ML)
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
2000 2200 2400 0200 0400 0600 0800 1000
CLOCK TIME (HR)

B


AMR-1 EXPERIMENT
NIGHT 2
TREATMENTS TERMINATED AT 0800
DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
LOG(x+1) MELATONIN (PG/ML)
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
2000 2200 2400 0200 0400 0600 0800 1000
CLOCK TIME (HR)


B
NIGHT 1
DLP-OC (n=8)
DLC-OC (n=8)
BLP-OC (n=8)
BLC-OC (n=8)
MELATONIN (PG/ML)
0
5
10
15
20
25
30
35
40
45
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

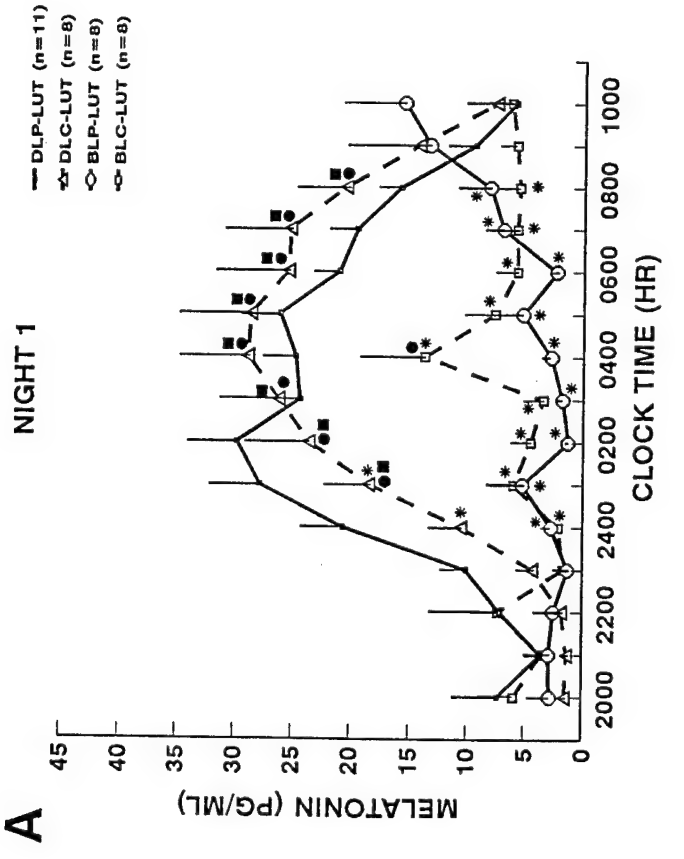
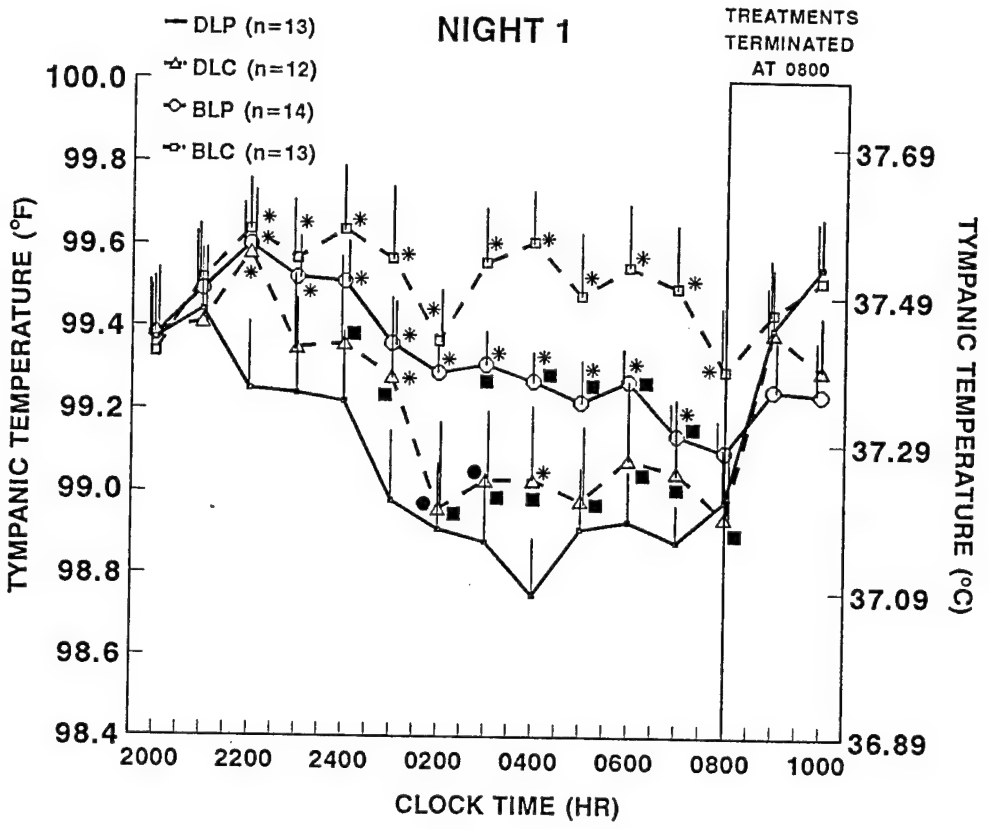
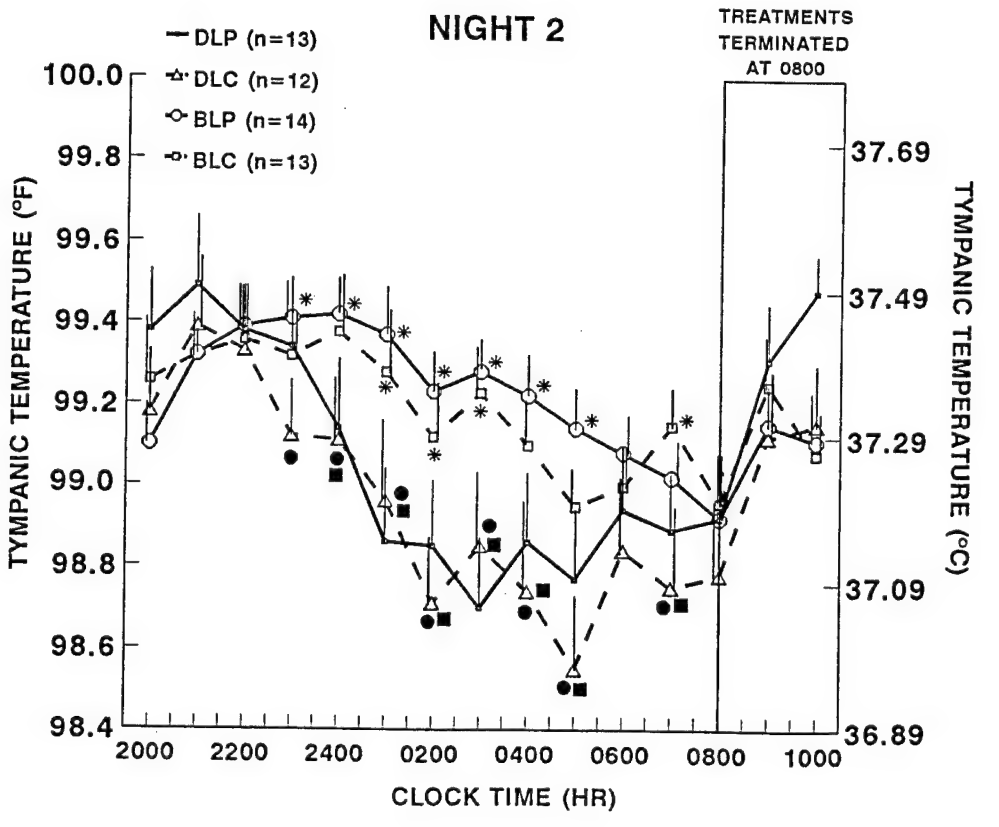

A
NIGHT 1
DLP-LUT (n=11)
DLC-LUT (n=8)
BLP-LUT (n=8)
BLC-LUT (n=8)
MELATONIN (PG/ML)
0
5
10
15
20
25
30
35
40
45
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

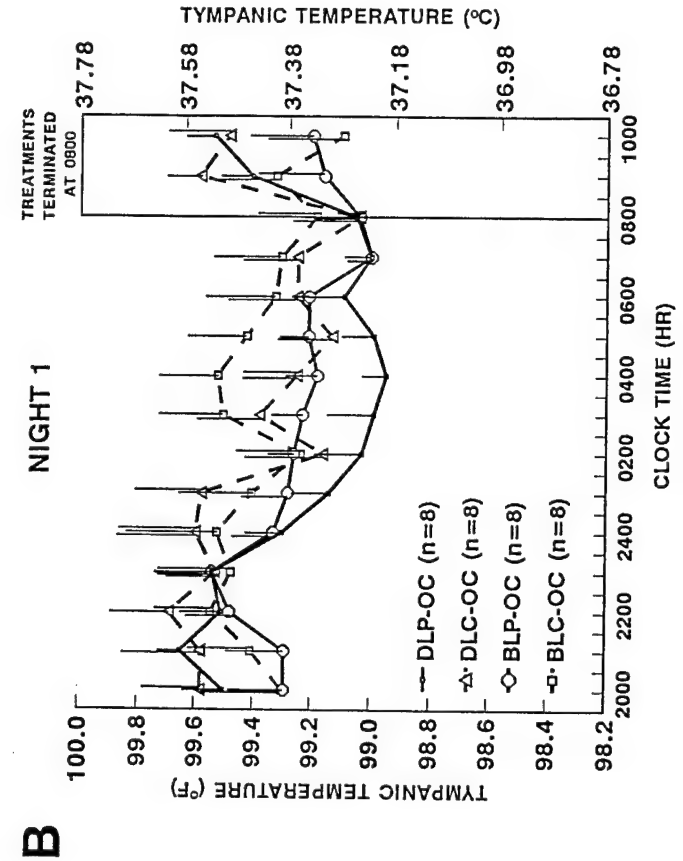
Figure 12

Figure 13 **A**


DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
NIGHT 1
TREATMENTS TERMINATED AT 0800
TYMPANIC TEMPERATURE (°F)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
TYMPANIC TEMPERATURE (°C)
37.69
37.49
37.29
37.09
36.89
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

B


DLP (n=13)
DLC (n=12)
BLP (n=14)
BLC (n=13)
NIGHT 2
TREATMENTS TERMINATED AT 0800
TYMPANIC TEMPERATURE (°F)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
TYMPANIC TEMPERATURE (°C)
37.69
37.49
37.29
37.09
36.89
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)


B
NIGHT 1
TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
TREATMENTS TERMINATED AT 0800
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
TYMPANIC TEMPERATURE (°F)
DLP-OC (n=8)
DLC-OC (n=8)
BLP-OC (n=8)
BLC-OC (n=8)
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

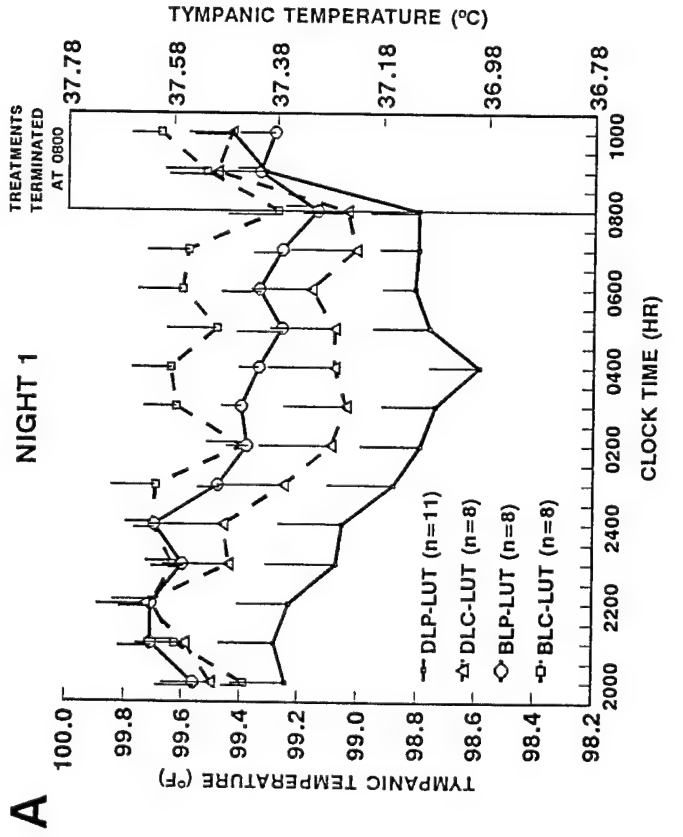
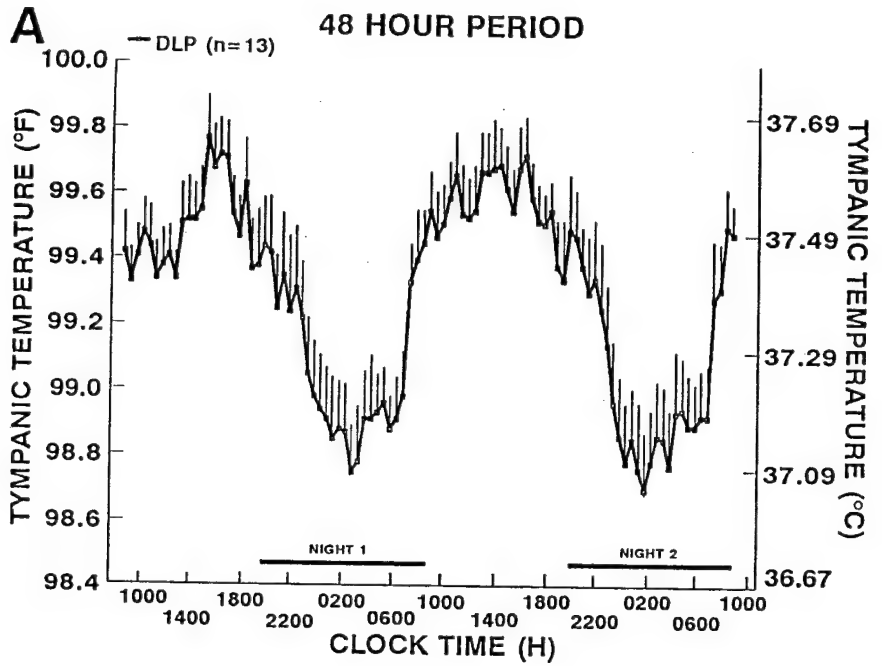
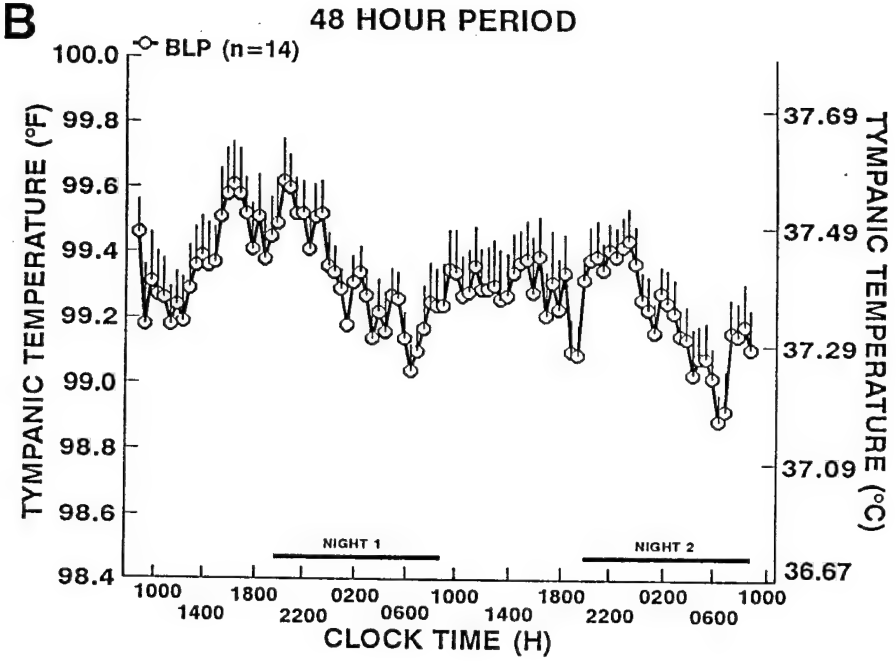
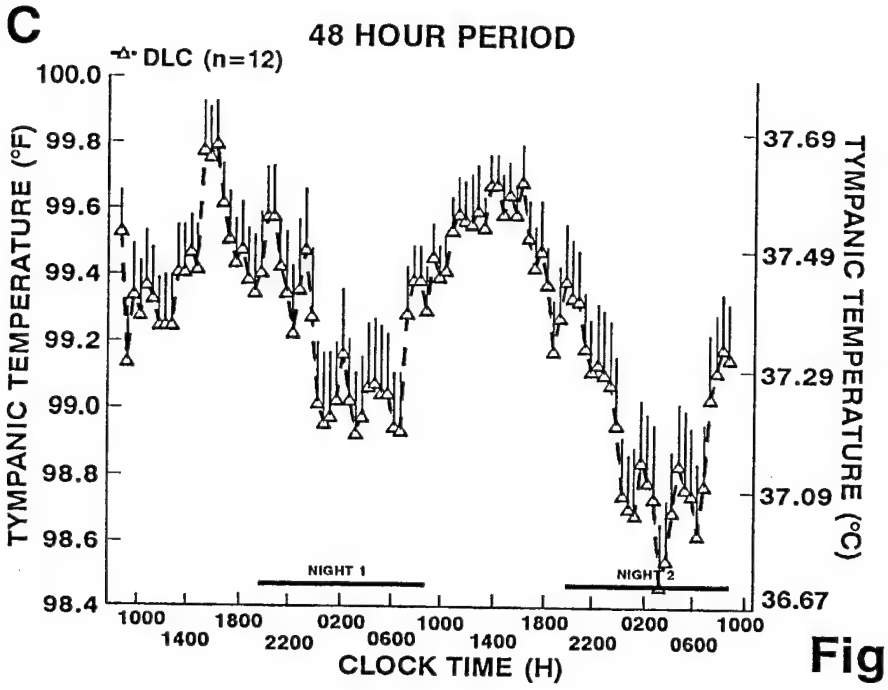

A
NIGHT 1
TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
TREATMENTS TERMINATED AT 0800
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
TYMPANIC TEMPERATURE (°F)
DLP-LUT (n=11)
DLC-LUT (n=8)
BLP-LUT (n=8)
BLC-LUT (n=8)
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

Figure 14







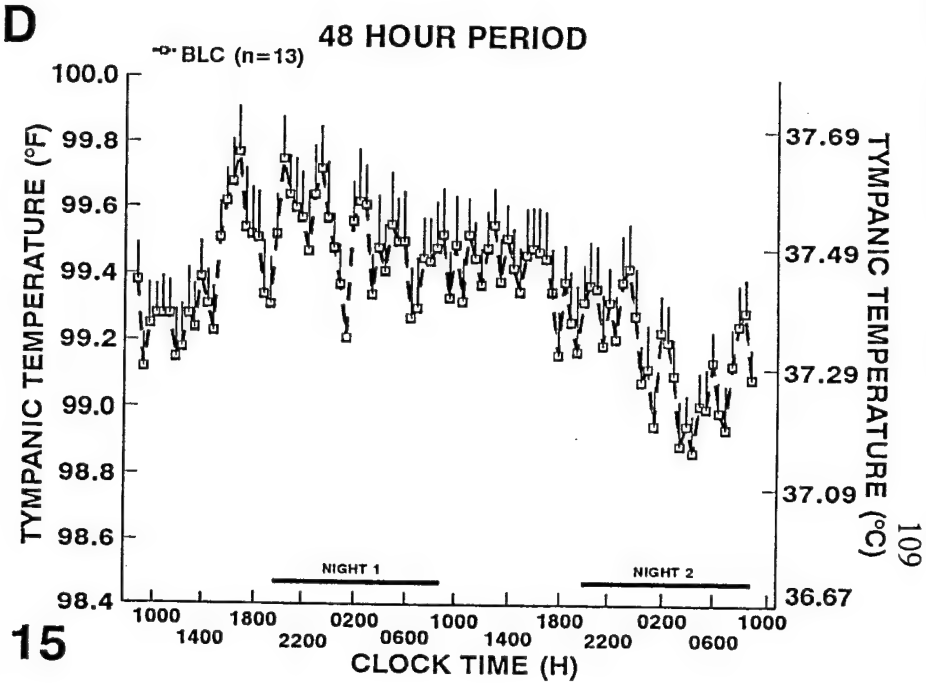
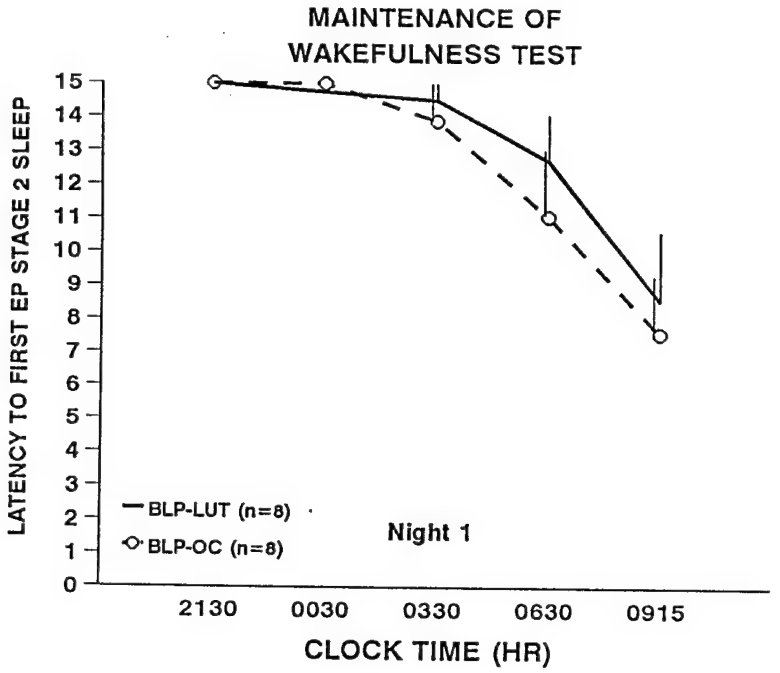
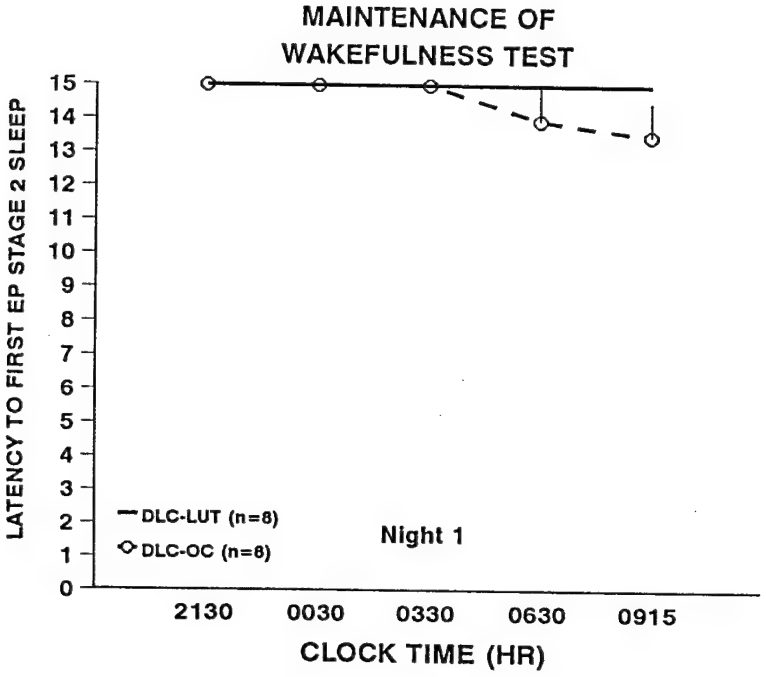


Figure 15

Cooperative Agreement No. DAMD17-95-2-5015

Figure 16


MAINTENANCE OF
WAKEFULNESS TEST
LATENCY TO FIRST EP STAGE 2 SLEEP
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
BLP-LUT (n=8)
BLP-OC (n=8)
Night 1
2130
0030
0330
0630
0915
CLOCK TIME (HR)


MAINTENANCE OF
WAKEFULNESS TEST
LATENCY TO FIRST EP STAGE 2 SLEEP
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
DLC-LUT (n=8)
DLC-OC (n=8)
Night 1
2130
0030
0330
0630
0915
CLOCK TIME (HR)

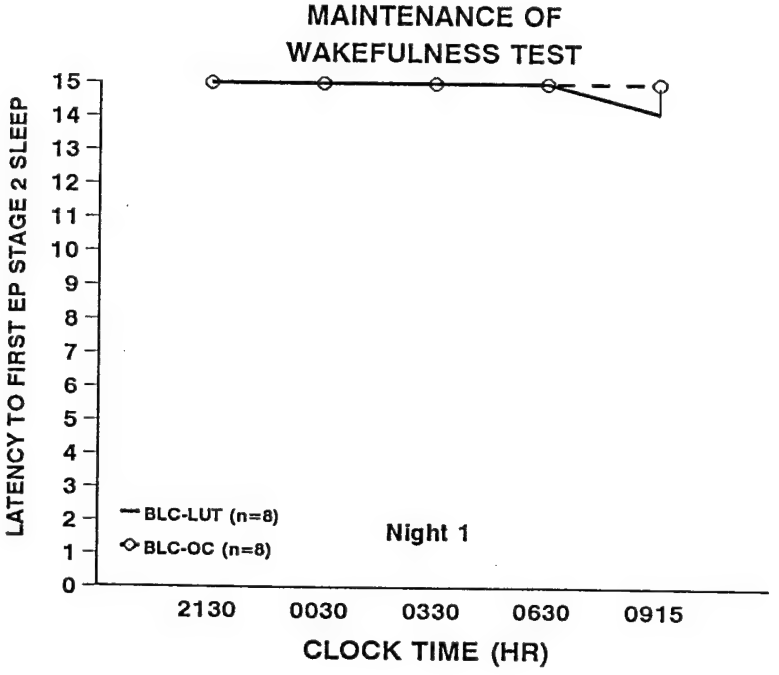
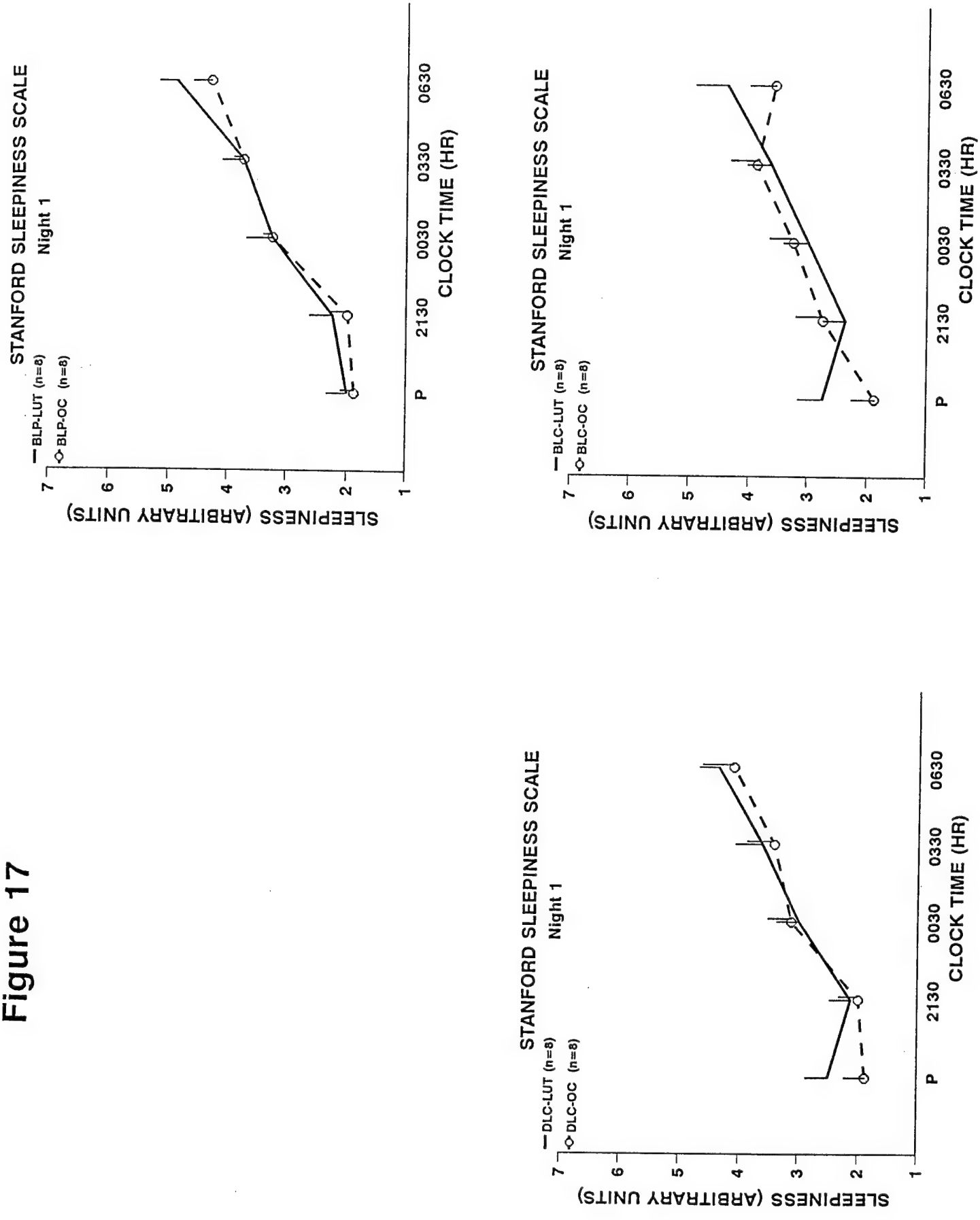
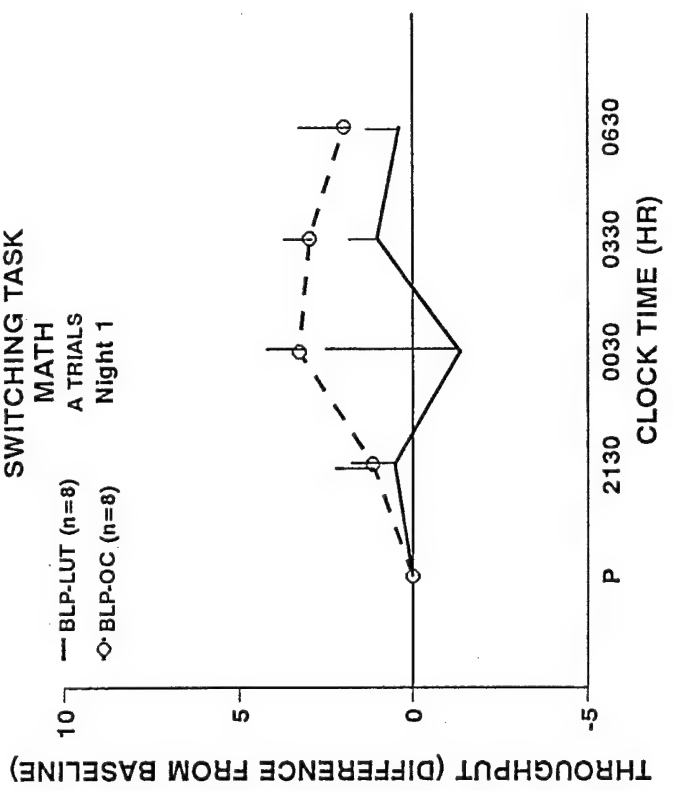
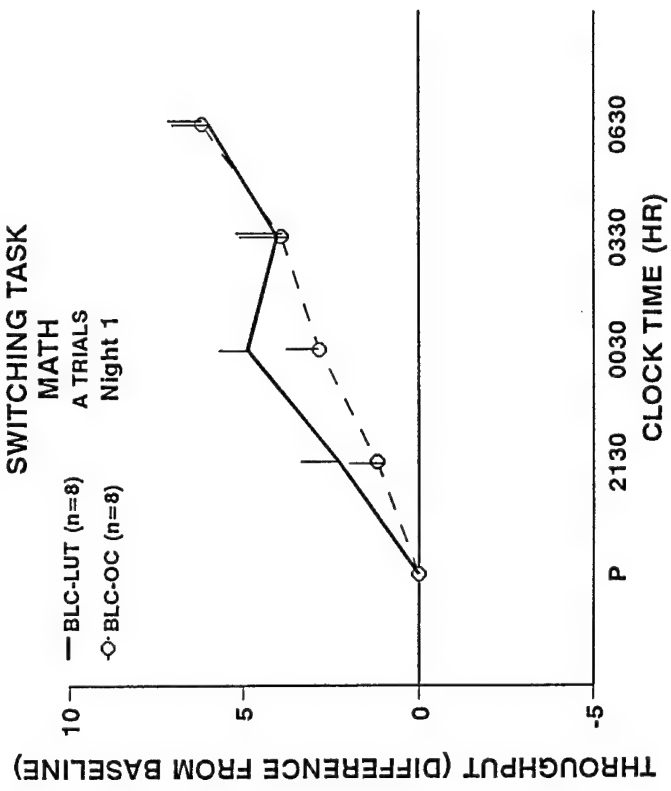

MAINTENANCE OF
WAKEFULNESS TEST
LATENCY TO FIRST EP STAGE 2 SLEEP
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
BLC-LUT (n=8)
BLC-OC (n=8)
Night 1
2130
0030
0330
0630
0915
CLOCK TIME (HR)

Figure 17


STANFORD SLEEPINESS SCALE
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
SLEEPINESS (ARBITRARY UNITS)
CLOCK TIME (HR)
P 2130 0030 0330 0630
STANFORD SLEEPINESS SCALE
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
SLEEPINESS (ARBITRARY UNITS)
CLOCK TIME (HR)
P 2130 0030 0330 0630
STANFORD SLEEPINESS SCALE
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
SLEEPINESS (ARBITRARY UNITS)
CLOCK TIME (HR)
P 2130 0030 0330 0630


SWITCHING TASK
MATH
A TRIALS
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)


SWITCHING TASK
MATH
A TRIALS
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

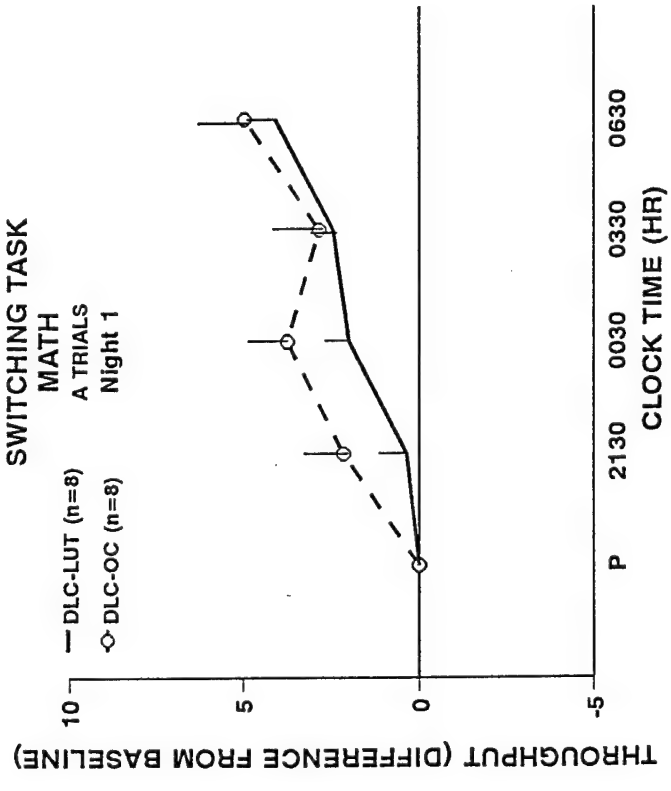
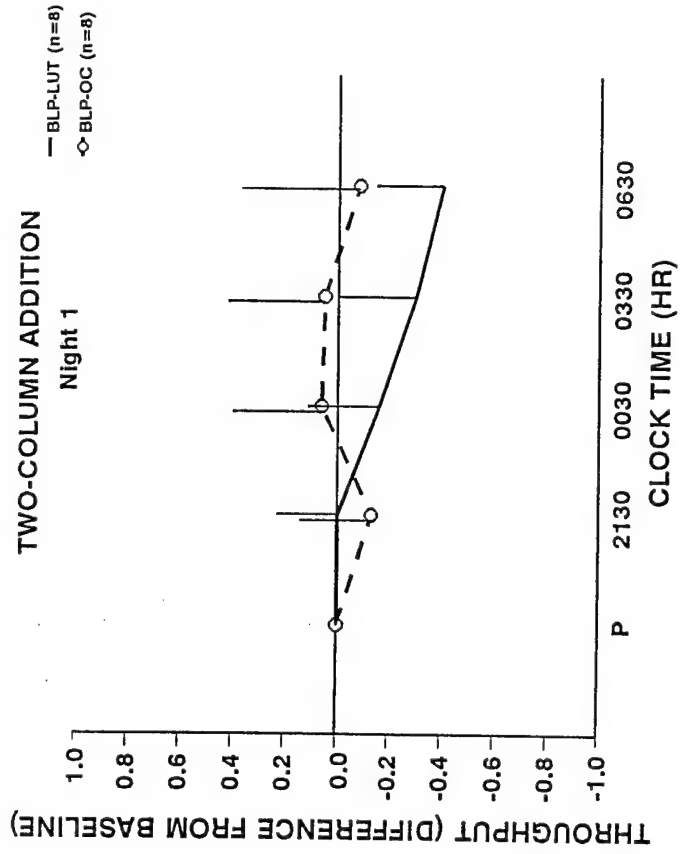
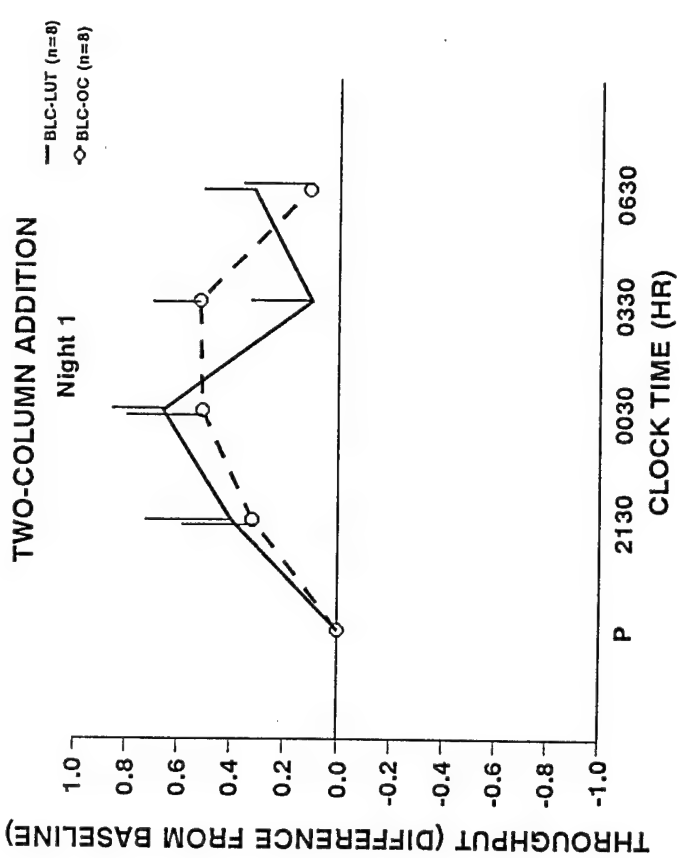

SWITCHING TASK
MATH
A TRIALS
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 18


TWO-COLUMN ADDITION
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
P
2130
0030
0330
0630
CLOCK TIME (HR)


TWO-COLUMN ADDITION
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
P
2130
0030
0330
0630
CLOCK TIME (HR)

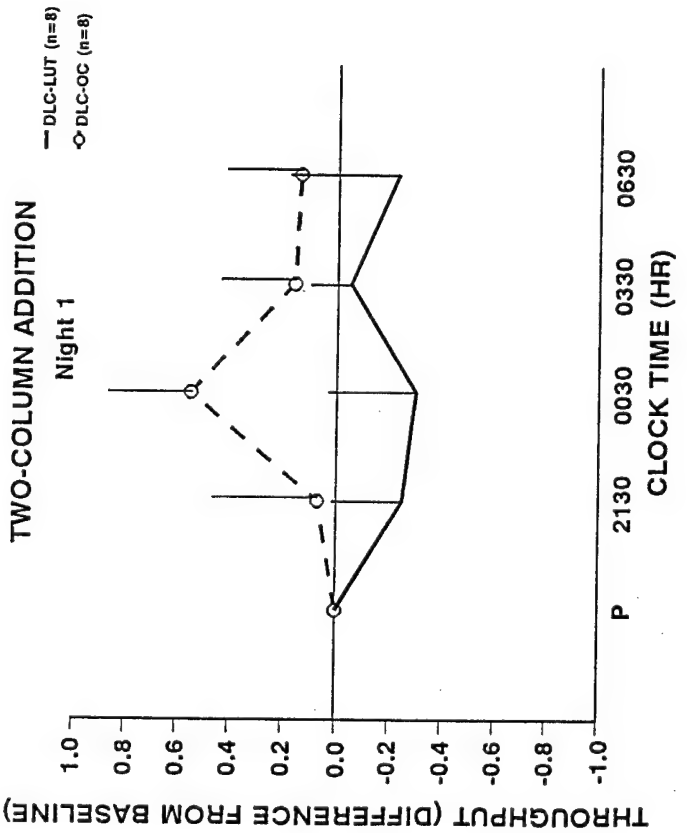
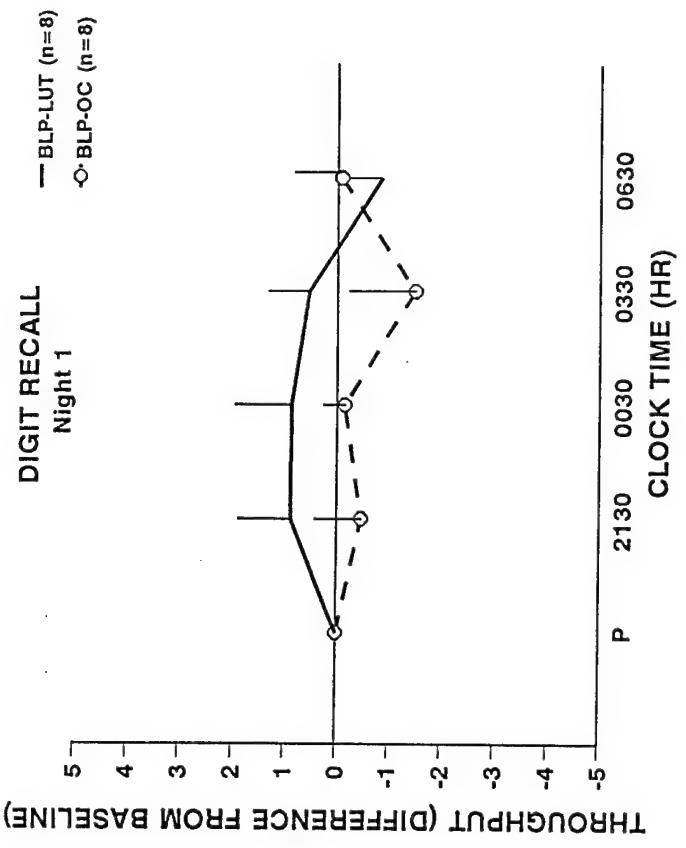
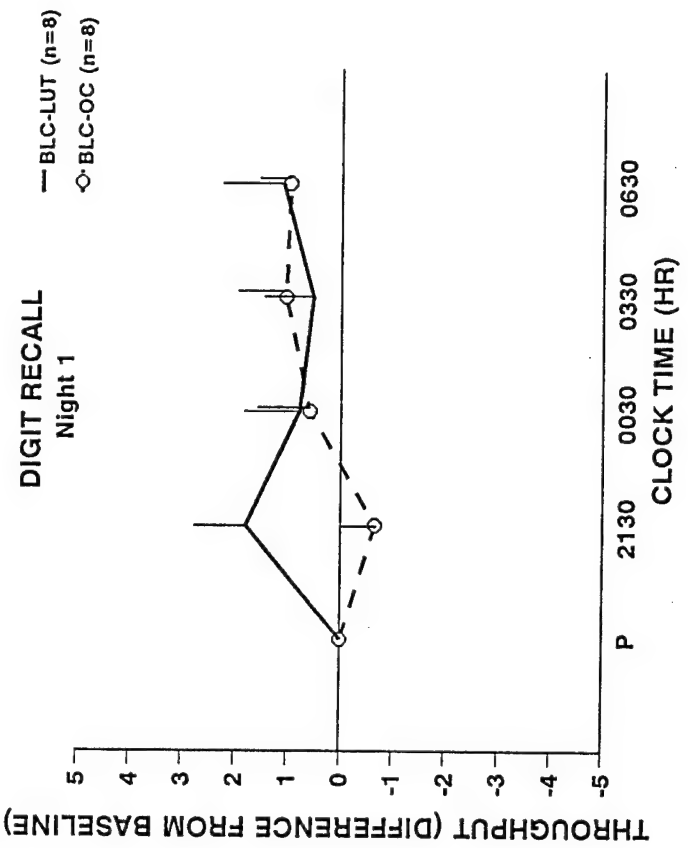

TWO-COLUMN ADDITION
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 19


DIGIT RECALL
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
5
4
3
2
1
0
-1
-2
-3
-4
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)


DIGIT RECALL
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
5
4
3
2
1
0
-1
-2
-3
-4
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

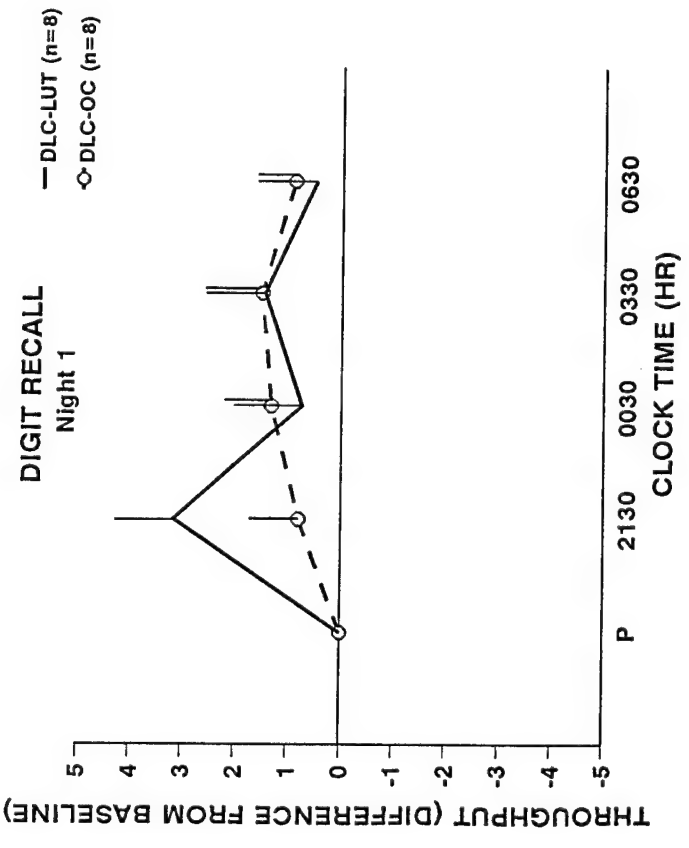
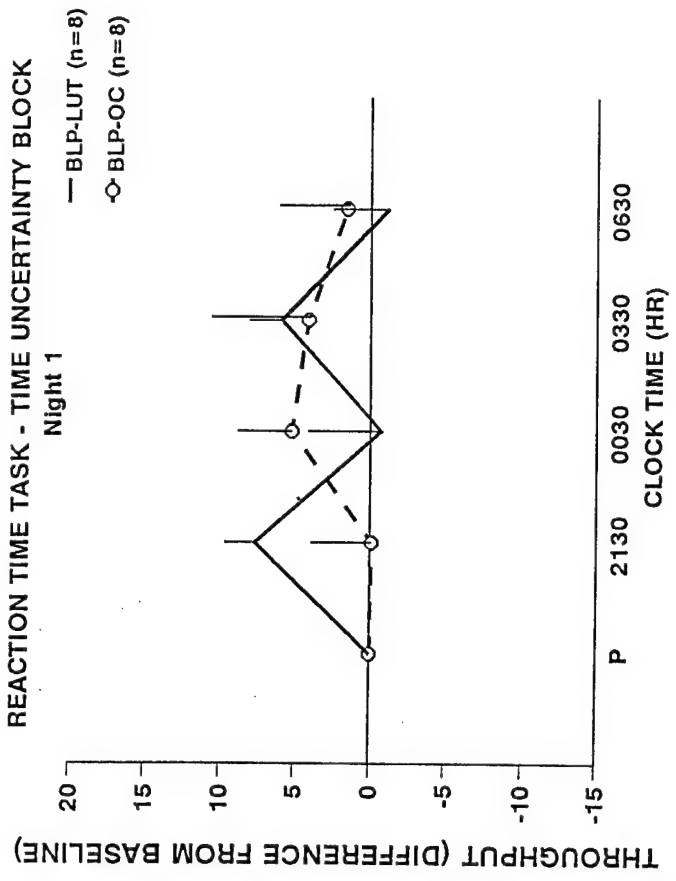

DIGIT RECALL
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
5
4
3
2
1
0
-1
-2
-3
-4
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 20


REACTION TIME TASK - TIME UNCERTAINTY BLOCK
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)

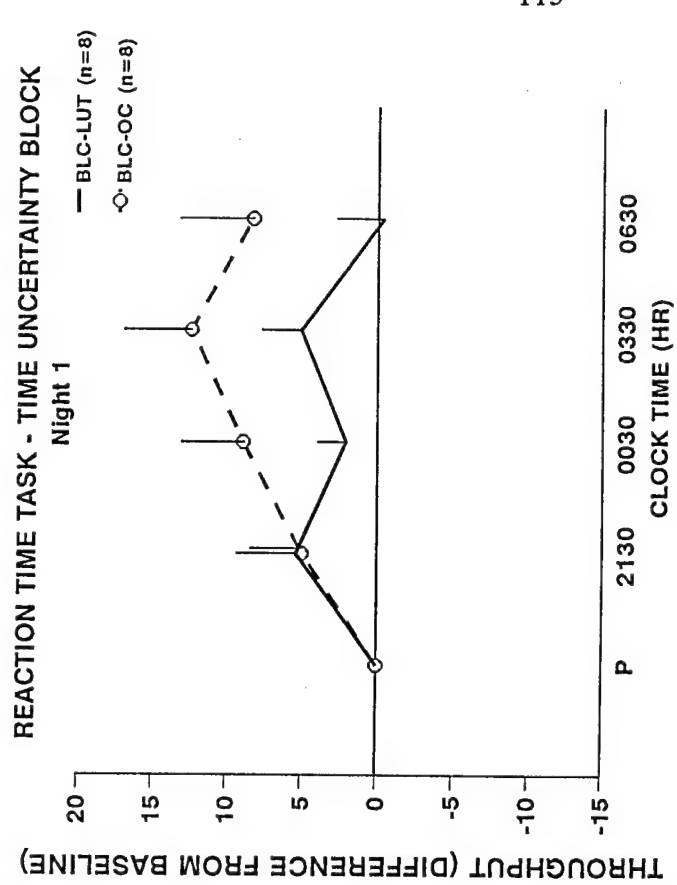
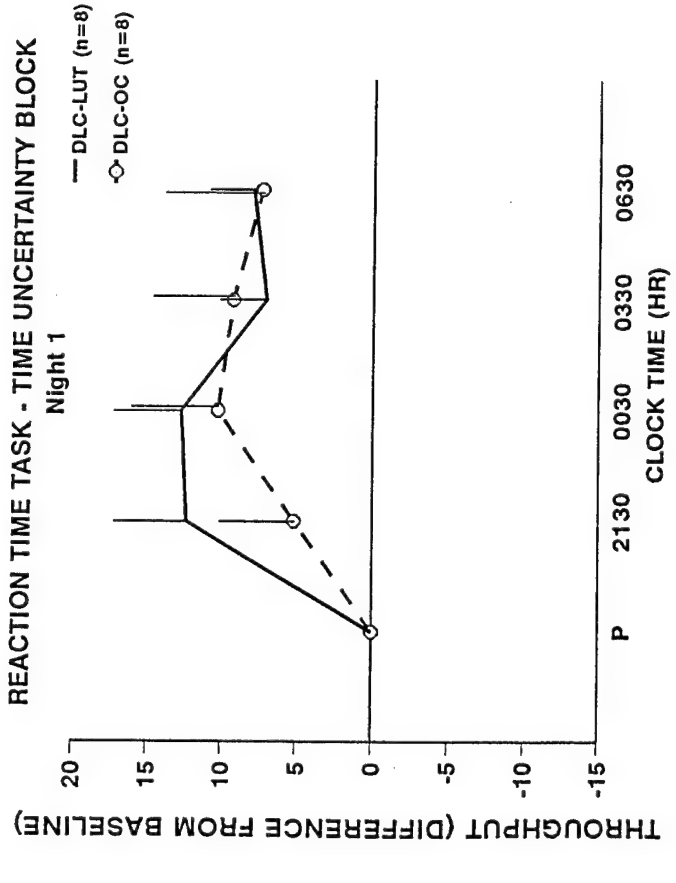
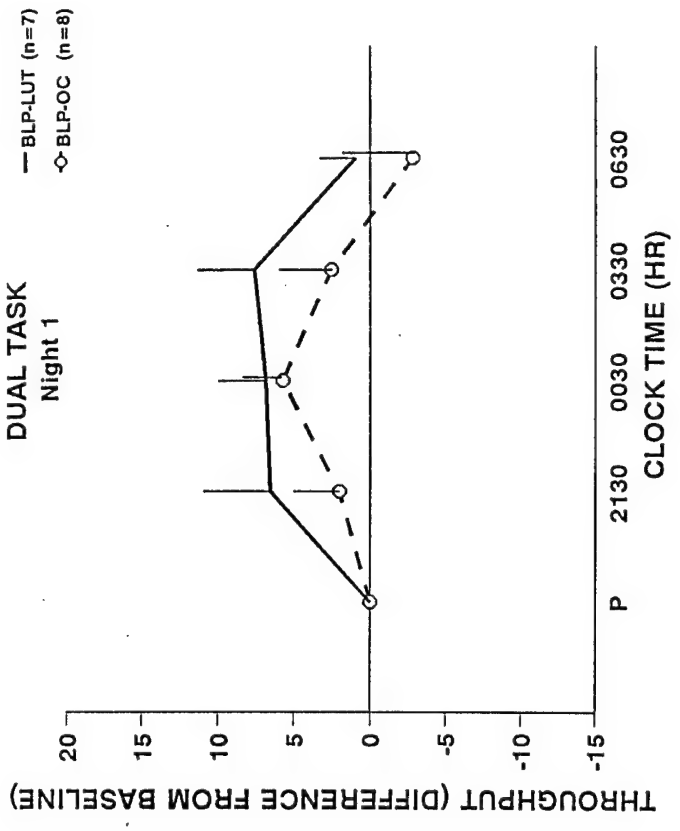
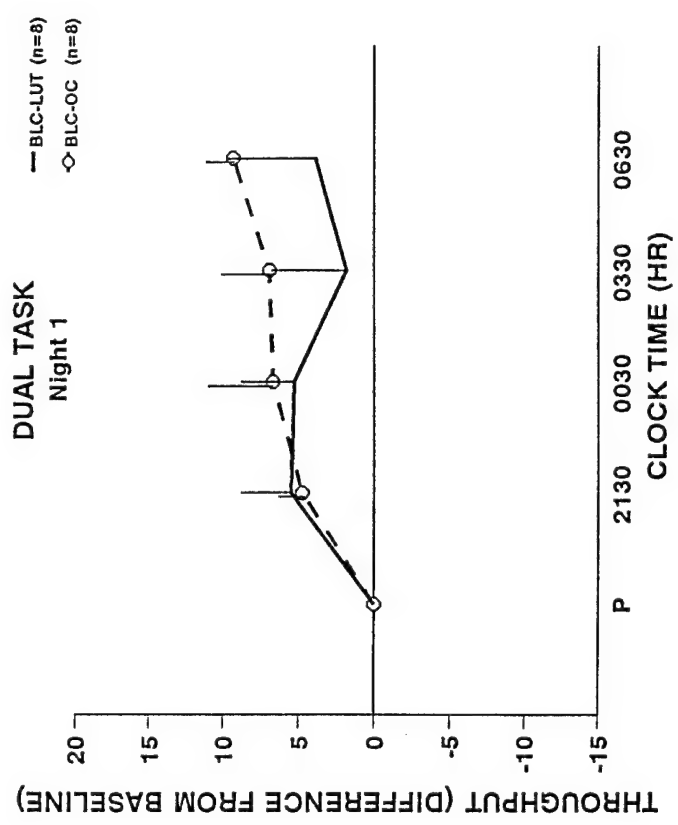

REACTION TIME TASK - TIME UNCERTAINTY BLOCK
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 21


REACTION TIME TASK - TIME UNCERTAINTY BLOCK
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)


DUAL TASK
Night 1
BLP-LUT (n=7)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)


DUAL TASK
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)

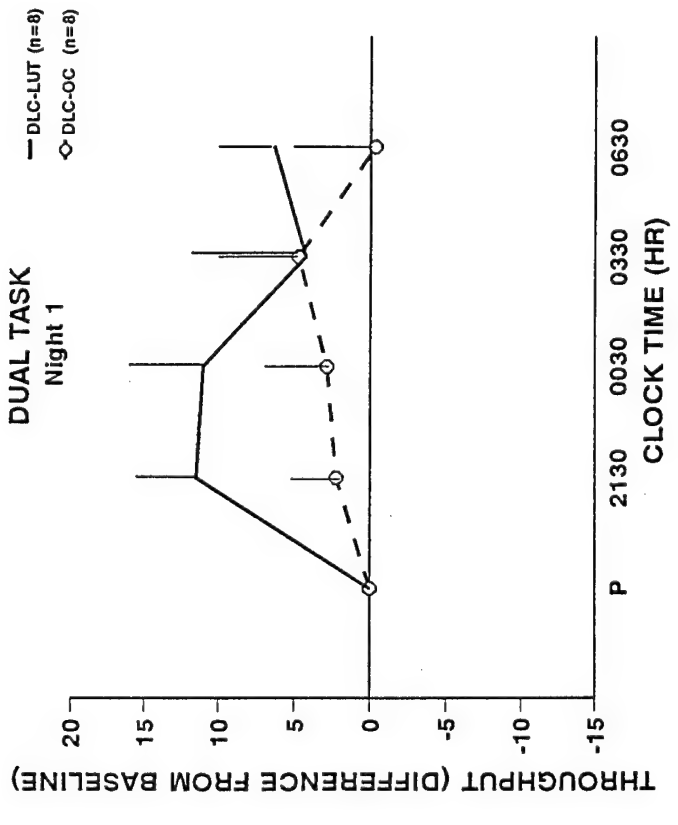
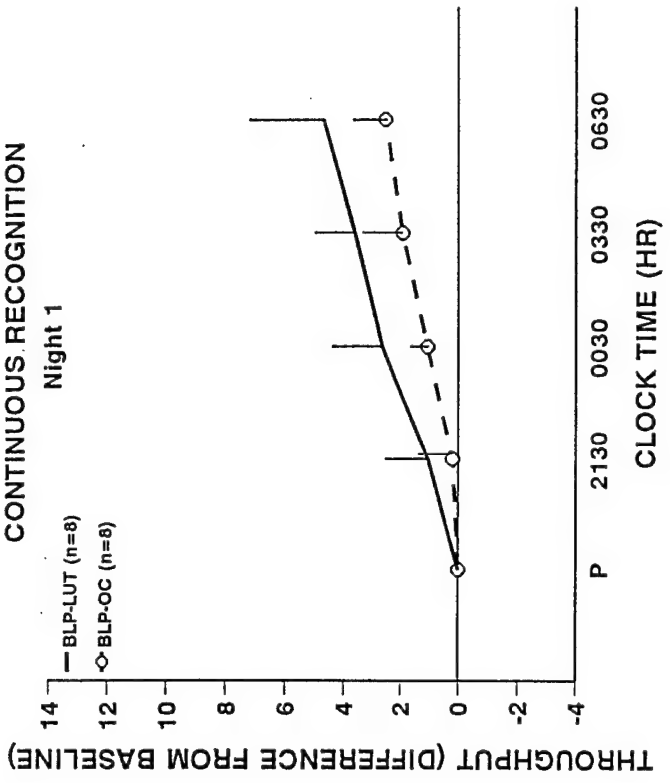
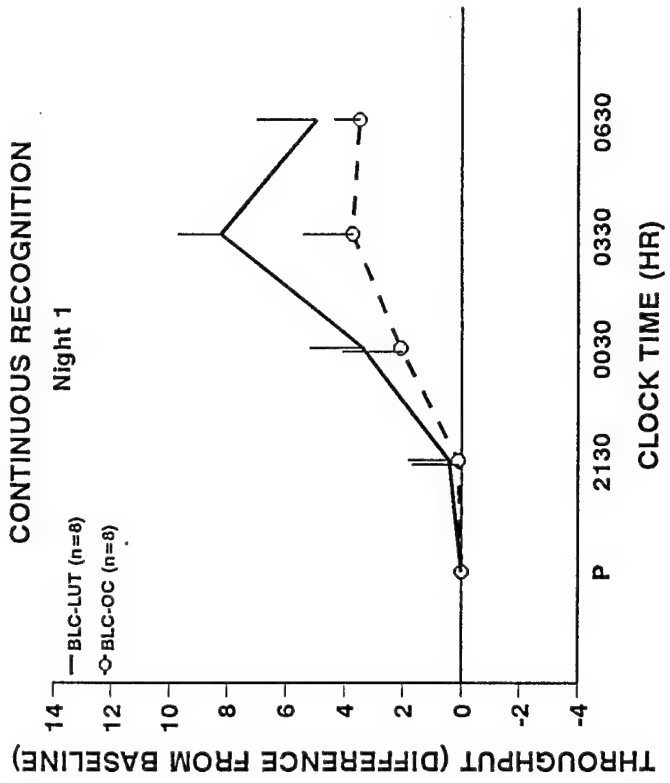

DUAL TASK
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 22


CONTINUOUS RECOGNITION
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
14
12
10
8
6
4
2
0
-2
-4
P
2130
0030
0330
0630
CLOCK TIME (HR)


CONTINUOUS RECOGNITION
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
14
12
10
8
6
4
2
0
-2
-4
P
2130
0030
0330
0630
CLOCK TIME (HR)

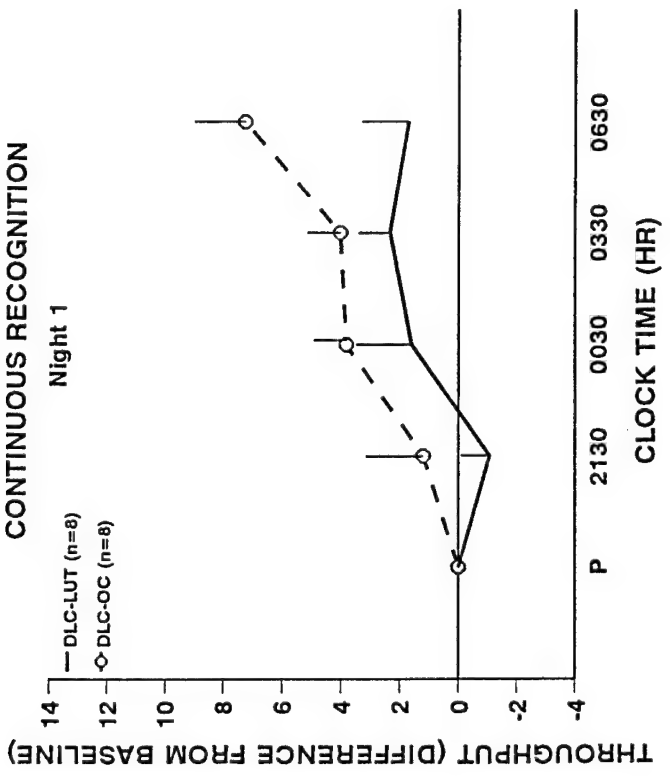
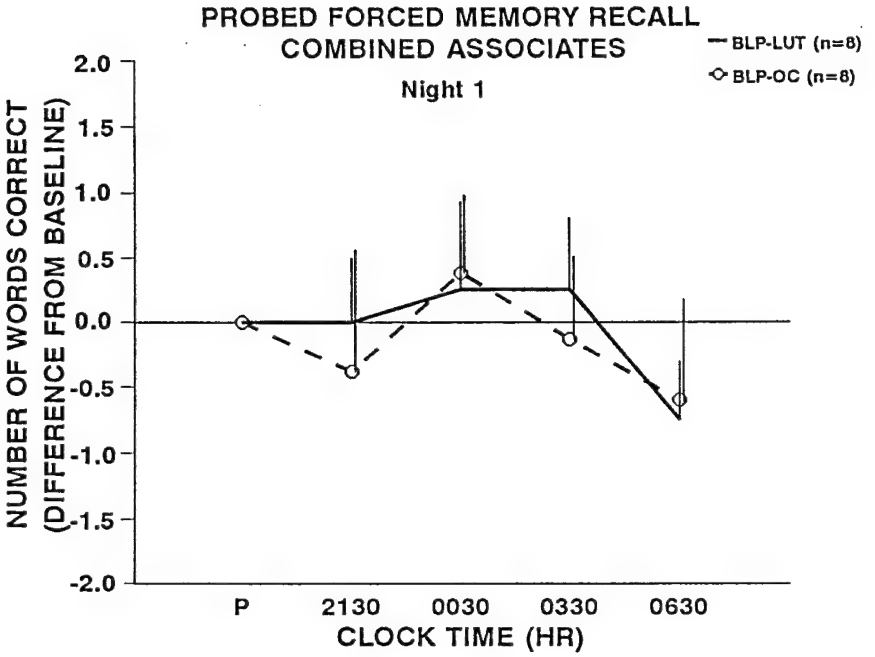
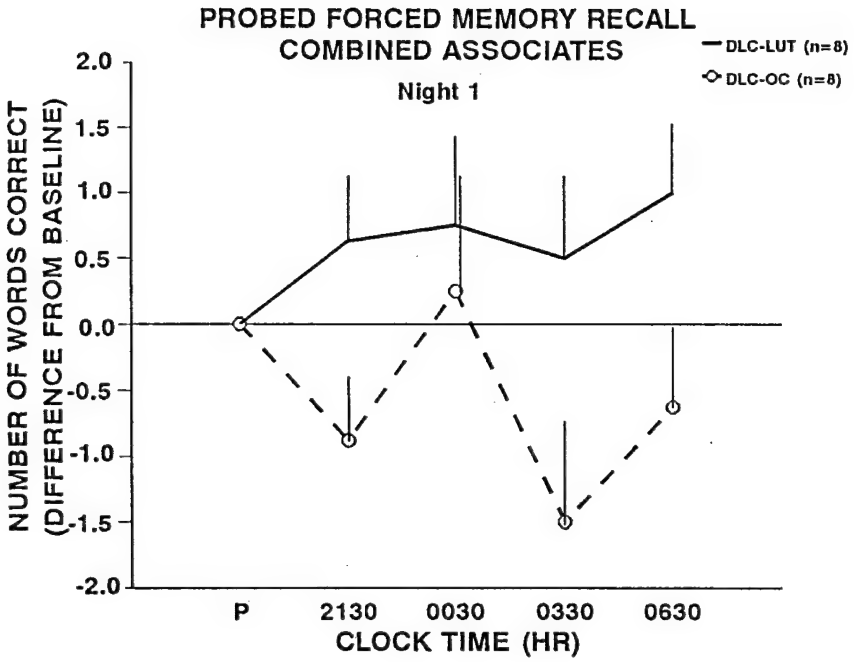
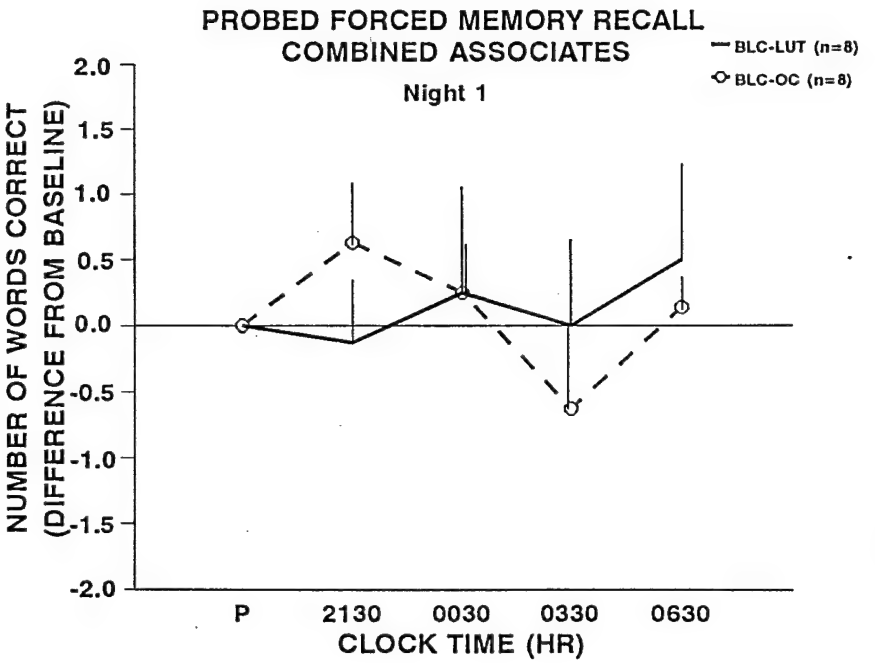

CONTINUOUS RECOGNITION
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
14
12
10
8
6
4
2
0
-2
-4
P
2130
0030
0330
0630
CLOCK TIME (HR)

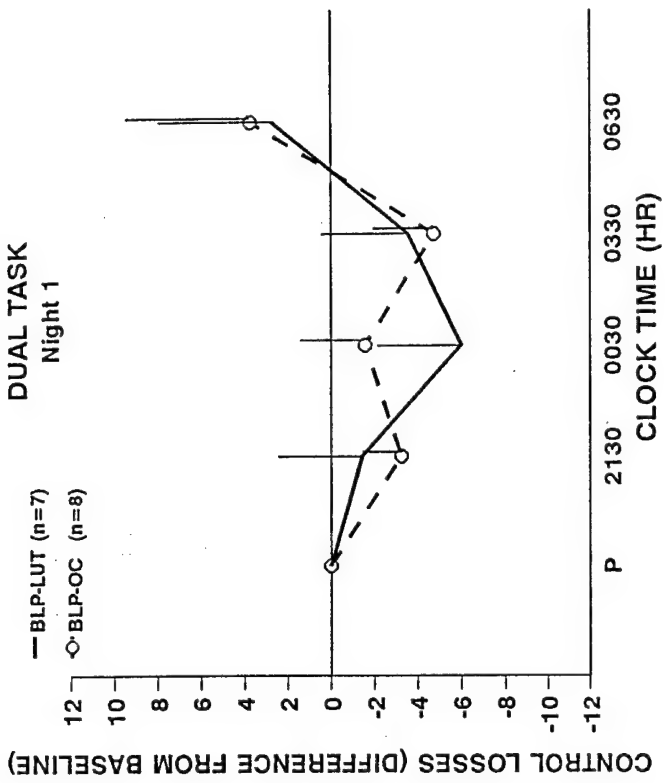
Figure 23

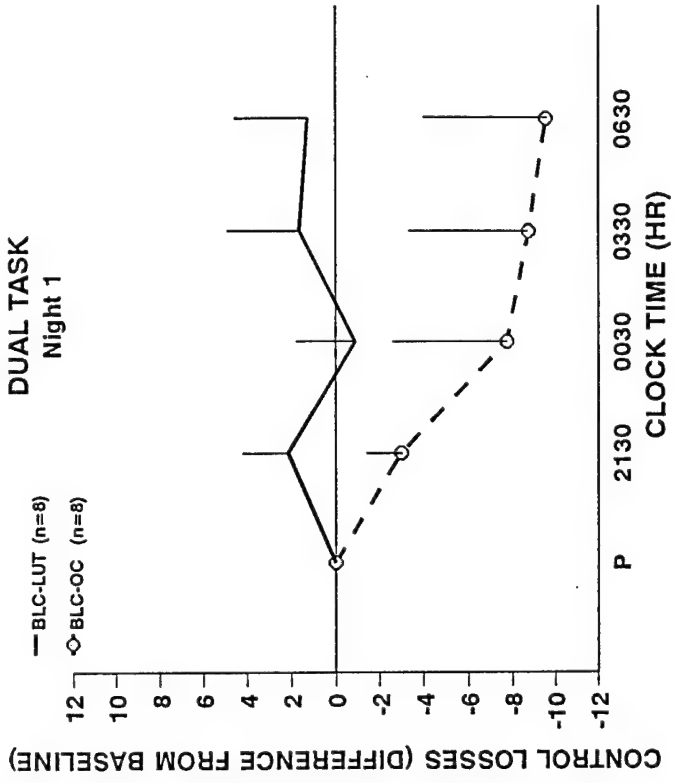
Figure 24


PROBED FORCED MEMORY RECALL
COMBINED ASSOCIATES
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
NUMBER OF WORDS CORRECT
(DIFFERENCE FROM BASELINE)
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
P
2130
0030
0330
0630
CLOCK TIME (HR)


PROBED FORCED MEMORY RECALL
COMBINED ASSOCIATES
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
NUMBER OF WORDS CORRECT
(DIFFERENCE FROM BASELINE)
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
P
2130
0030
0330
0630
CLOCK TIME (HR)


PROBED FORCED MEMORY RECALL
COMBINED ASSOCIATES
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
NUMBER OF WORDS CORRECT
(DIFFERENCE FROM BASELINE)
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
P
2130
0030
0330
0630
CLOCK TIME (HR)


DUAL TASK
Night 1
BLP-LUT (n=7)
BLP-OC (n=8)
CONTROL LOSSES (DIFFERENCE FROM BASELINE)
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
-12
P
2130
0030
0330
0630
CLOCK TIME (HR)


DUAL TASK
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
CONTROL LOSSES (DIFFERENCE FROM BASELINE)
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
-12
P
2130
0030
0330
0630
CLOCK TIME (HR)

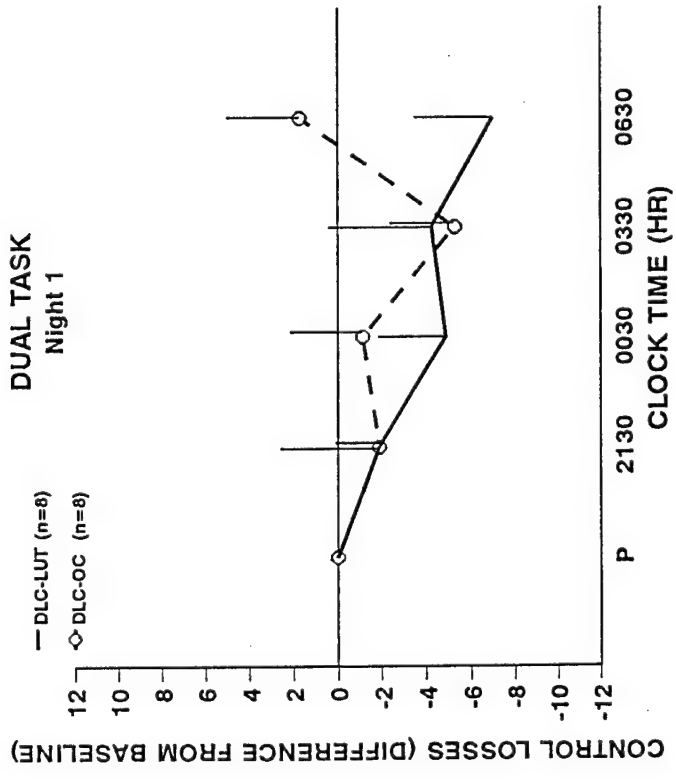
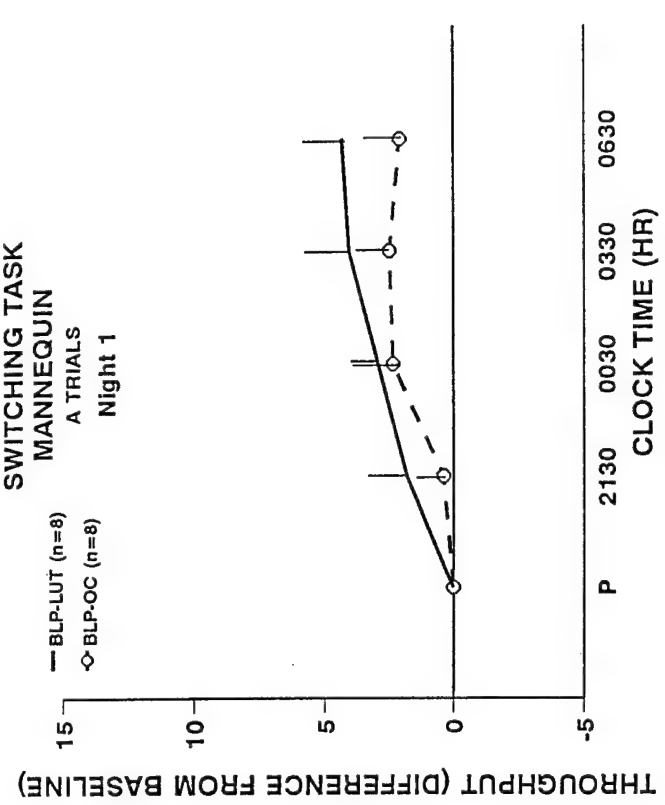

DUAL TASK
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
CONTROL LOSSES (DIFFERENCE FROM BASELINE)
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
-12
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 25


SWITCHING TASK
MANNEQUIN
A TRIALS
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
15
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

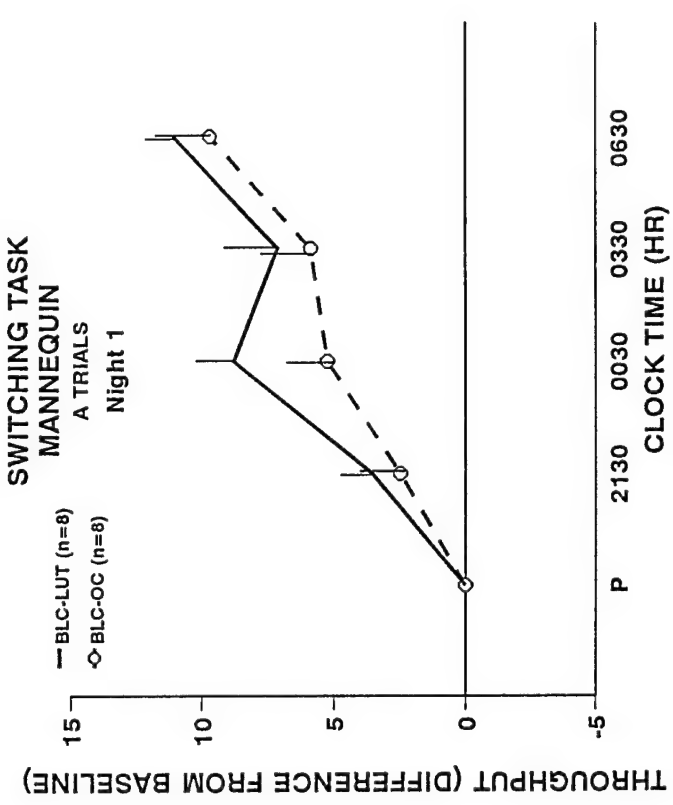

SWITCHING TASK
MANNEQUIN
A TRIALS
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
15
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 26

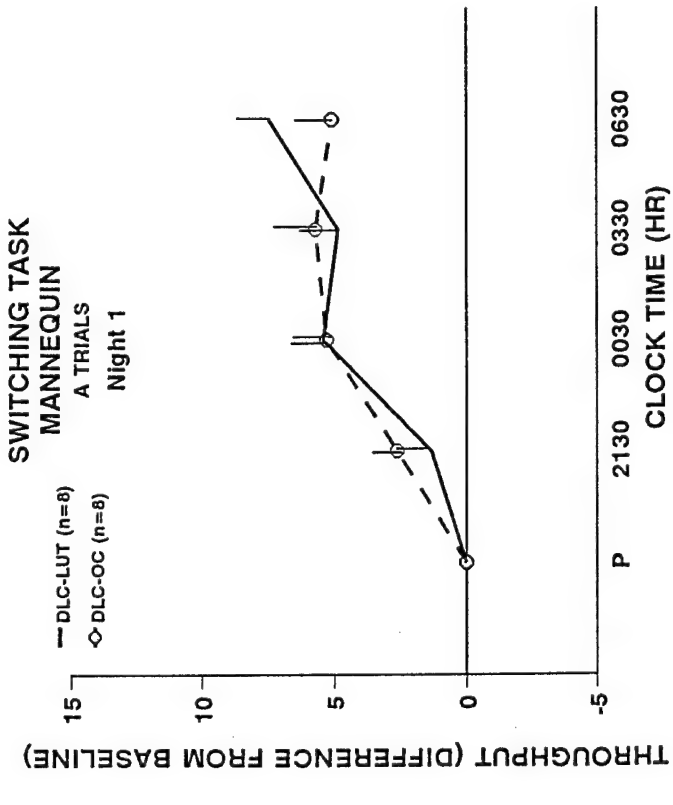
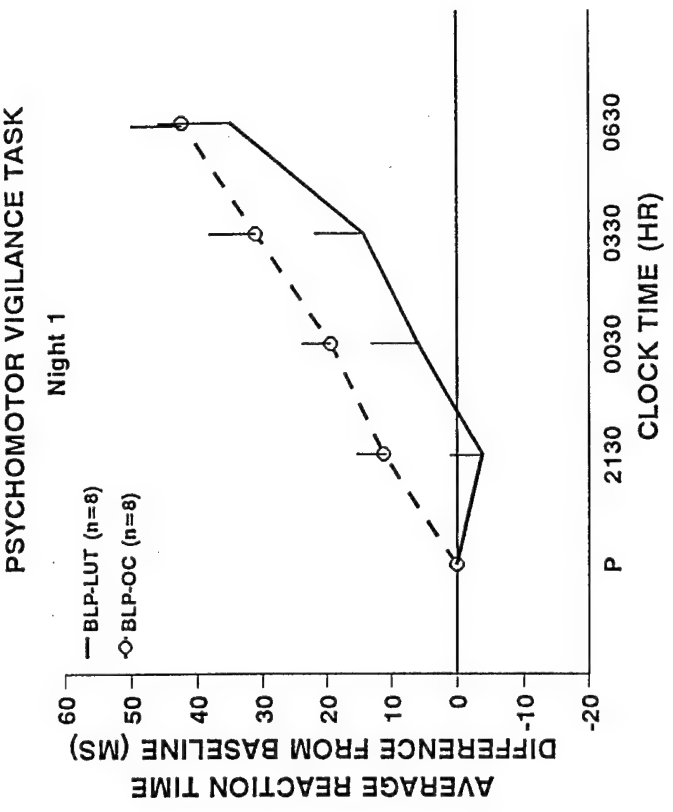
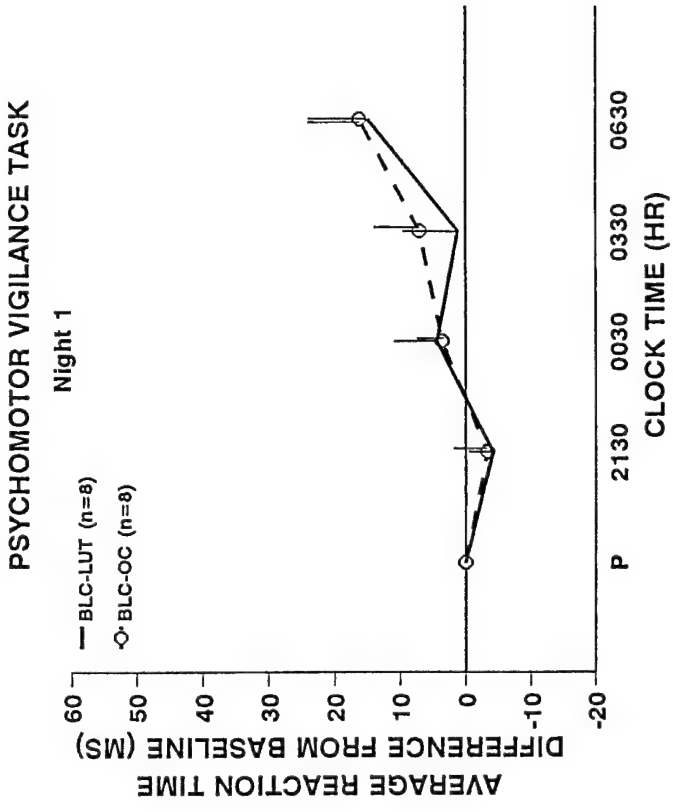
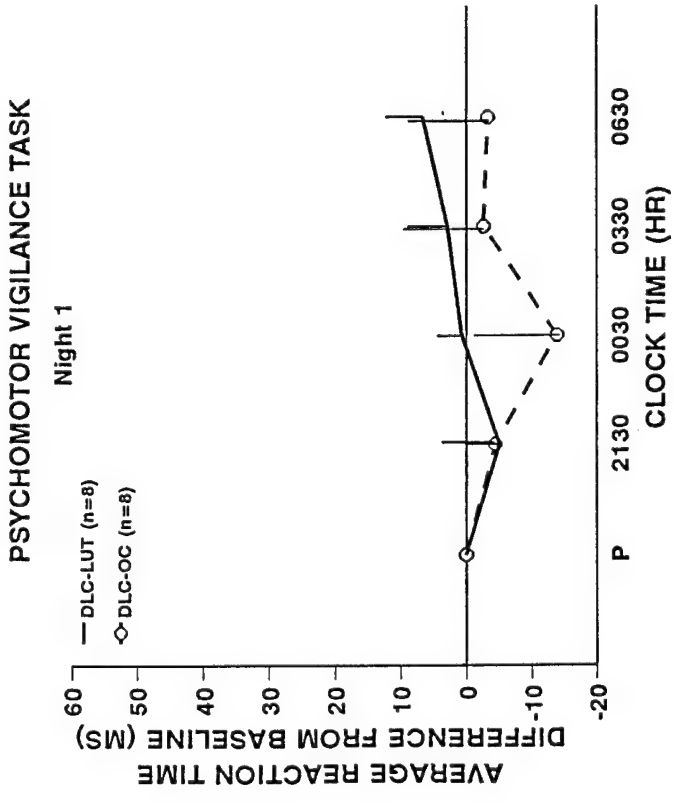
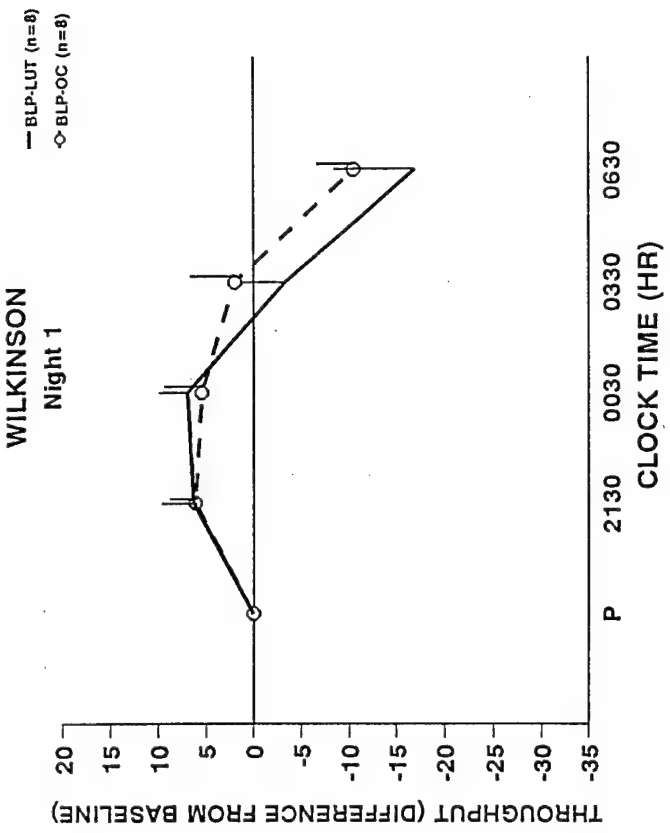

SWITCHING TASK
MANNEQUIN
A TRIALS
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
15
10
5
0
-5
P
2130
0030
0330
0630
CLOCK TIME (HR)

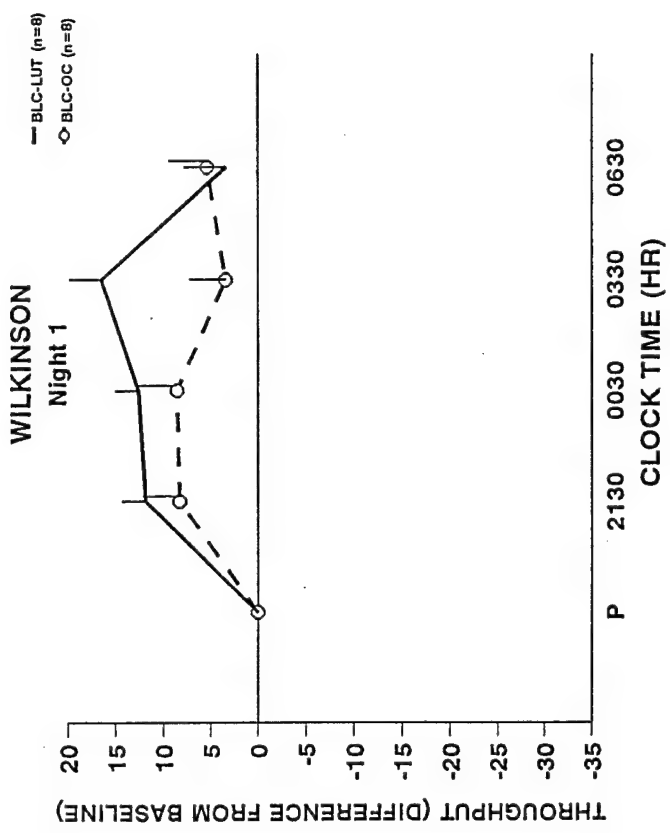
Figure 27


PSYCHOMOTOR VIGILANCE TASK
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
AVERAGE REACTION TIME DIFFERENCE FROM BASELINE (MS)
60
50
40
30
20
10
0
-10
-20
P
2130
0030
0330
0630
CLOCK TIME (HR)


PSYCHOMOTOR VIGILANCE TASK
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
AVERAGE REACTION TIME DIFFERENCE FROM BASELINE (MS)
60
50
40
30
20
10
0
-10
-20
P
2130
0030
0330
0630
CLOCK TIME (HR)


PSYCHOMOTOR VIGILANCE TASK
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
AVERAGE REACTION TIME DIFFERENCE FROM BASELINE (MS)
60
50
40
30
20
10
0
-10
-20
P
2130
0030
0330
0630
CLOCK TIME (HR)


WILKINSON
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
P
2130
0030
0330
0630
CLOCK TIME (HR)


WILKINSON
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
P
2130
0030
0330
0630
CLOCK TIME (HR)

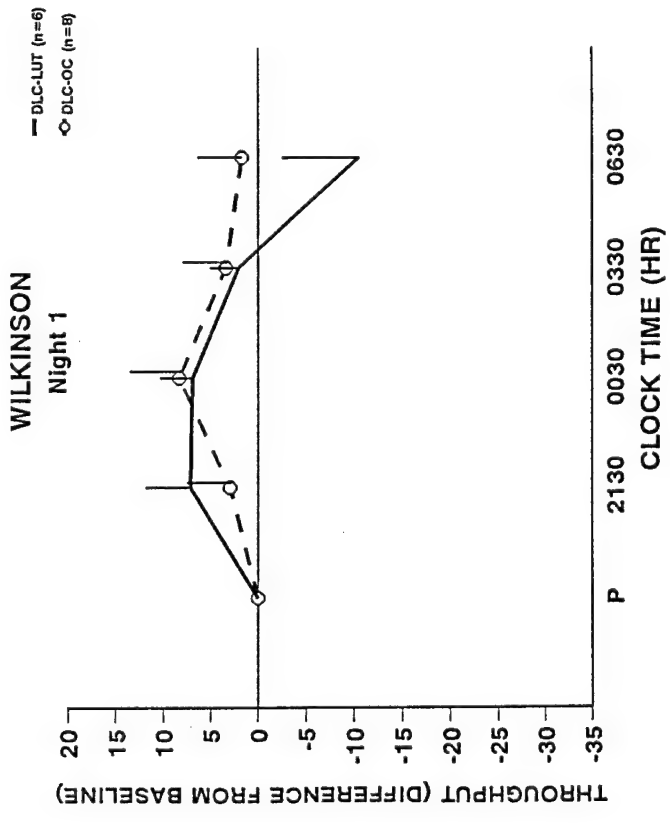

WILKINSON
Night 1
DLC-LUT (n=6)
DLC-OC (n=8)
THROUGHPUT (DIFFERENCE FROM BASELINE)
20
15
10
5
0
-5
-10
-15
-20
-25
-30
-35
P
2130
0030
0330
0630
CLOCK TIME (HR)

Figure 28

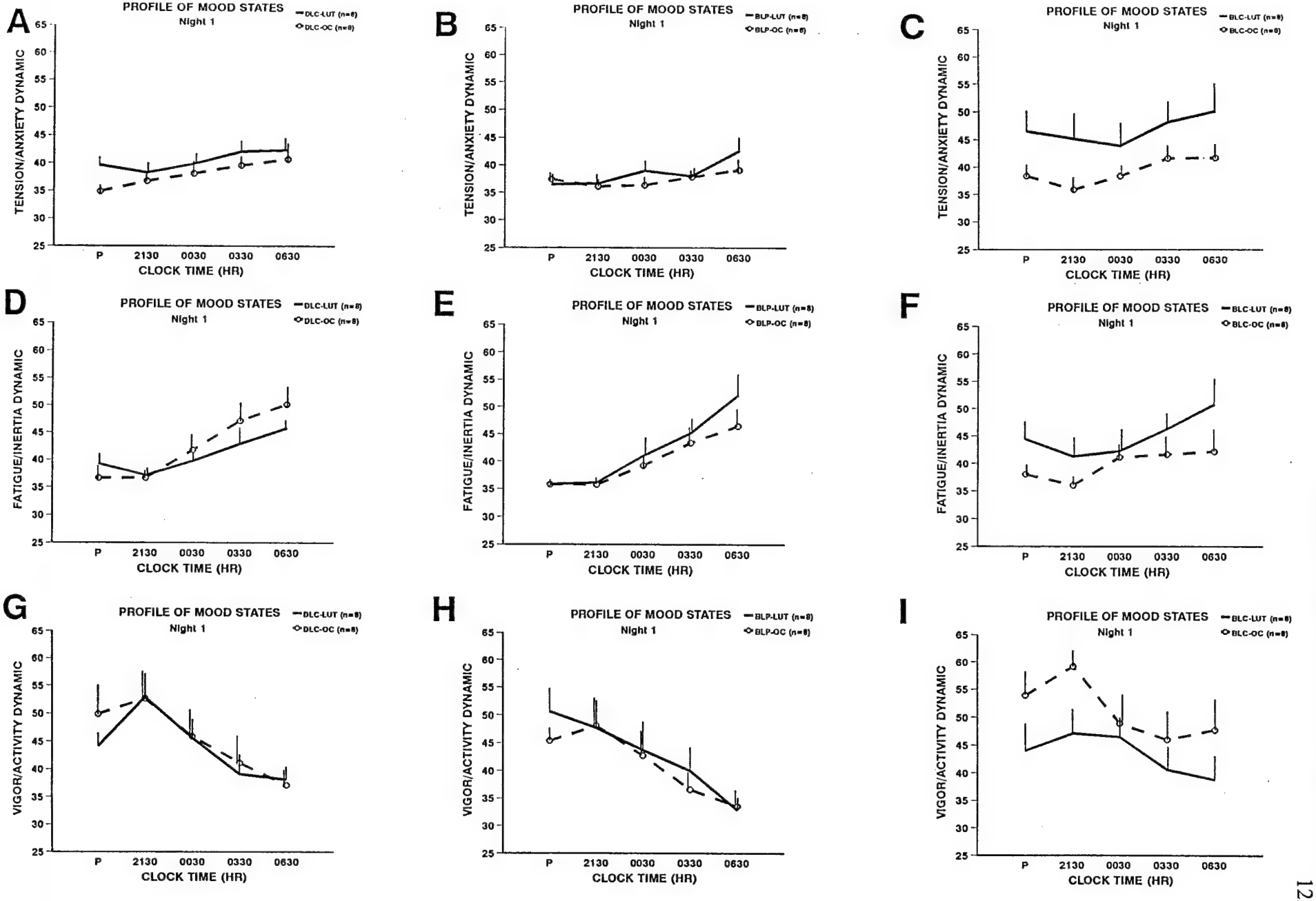

A
PROFILE OF MOOD STATES
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
TENSION/ANXIETY DYNAMIC
CLOCK TIME (HR)
B
PROFILE OF MOOD STATES
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
TENSION/ANXIETY DYNAMIC
CLOCK TIME (HR)
C
PROFILE OF MOOD STATES
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
TENSION/ANXIETY DYNAMIC
CLOCK TIME (HR)
D
PROFILE OF MOOD STATES
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
FATIGUE/INERTIA DYNAMIC
CLOCK TIME (HR)
E
PROFILE OF MOOD STATES
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
FATIGUE/INERTIA DYNAMIC
CLOCK TIME (HR)
F
PROFILE OF MOOD STATES
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
FATIGUE/INERTIA DYNAMIC
CLOCK TIME (HR)
G
PROFILE OF MOOD STATES
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
VIGOR/ACTIVITY DYNAMIC
CLOCK TIME (HR)
H
PROFILE OF MOOD STATES
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
VIGOR/ACTIVITY DYNAMIC
CLOCK TIME (HR)
I
PROFILE OF MOOD STATES
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
VIGOR/ACTIVITY DYNAMIC
CLOCK TIME (HR)
P
2130
0030
0330
0630

Figure 29

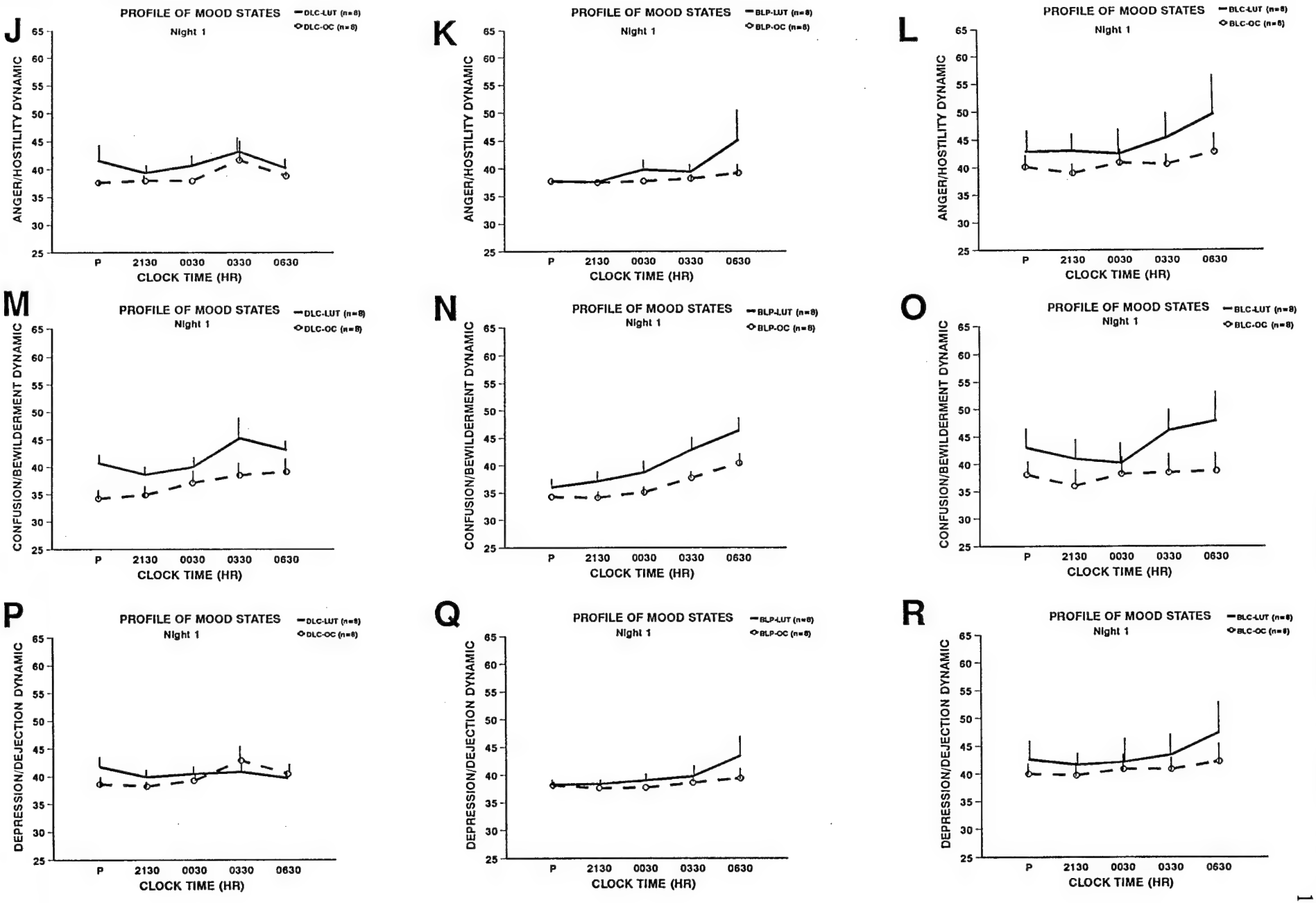
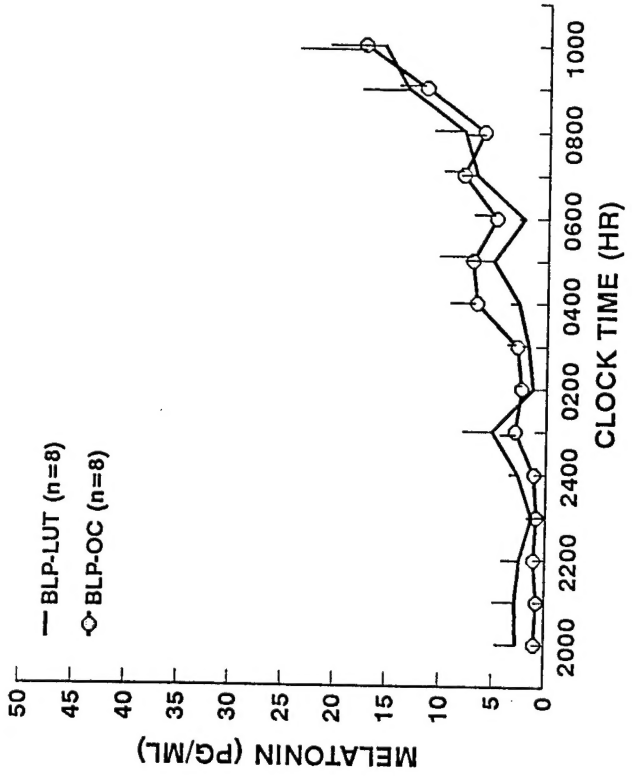
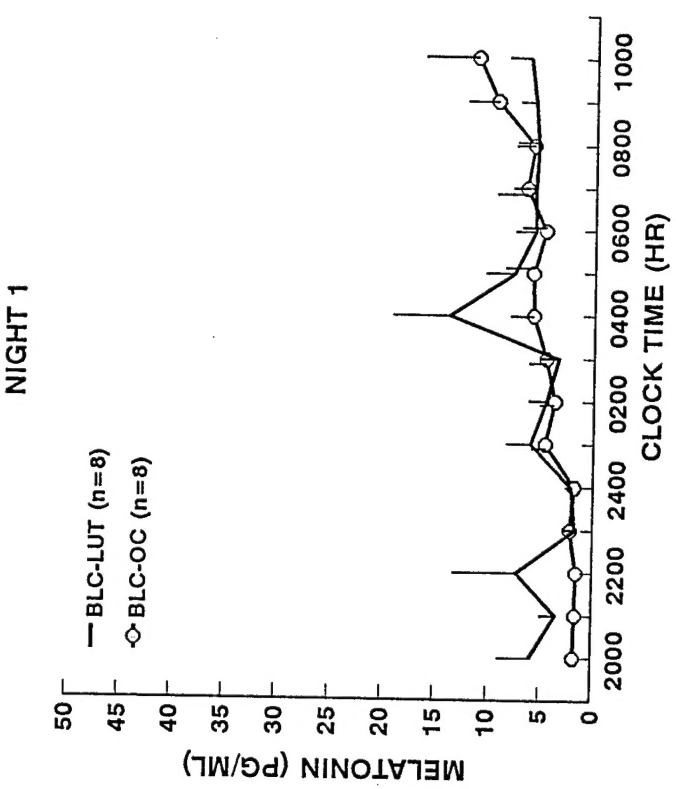

J
PROFILE OF MOOD STATES
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
ANGER/HOSTILITY DYNAMIC
CLOCK TIME (HR)
K
PROFILE OF MOOD STATES
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
ANGER/HOSTILITY DYNAMIC
CLOCK TIME (HR)
L
PROFILE OF MOOD STATES
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
ANGER/HOSTILITY DYNAMIC
CLOCK TIME (HR)
M
PROFILE OF MOOD STATES
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
CONFUSION/BEWILDERMENT DYNAMIC
CLOCK TIME (HR)
N
PROFILE OF MOOD STATES
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
CONFUSION/BEWILDERMENT DYNAMIC
CLOCK TIME (HR)
O
PROFILE OF MOOD STATES
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
CONFUSION/BEWILDERMENT DYNAMIC
CLOCK TIME (HR)
P
PROFILE OF MOOD STATES
Night 1
DLC-LUT (n=8)
DLC-OC (n=8)
DEPRESSION/DEJECTION DYNAMIC
CLOCK TIME (HR)
Q
PROFILE OF MOOD STATES
Night 1
BLP-LUT (n=8)
BLP-OC (n=8)
DEPRESSION/DEJECTION DYNAMIC
CLOCK TIME (HR)
R
PROFILE OF MOOD STATES
Night 1
BLC-LUT (n=8)
BLC-OC (n=8)
DEPRESSION/DEJECTION DYNAMIC
CLOCK TIME (HR)
P
2130
0030
0330
0630

Figure 29

Figure 30


NIGHT 1
BLP-LUT (n=8)
BLP-OC (n=8)
MELATONIN (PG/ML)
CLOCK TIME (HR)
0
5
10
15
20
25
30
35
40
45
50
2000
2200
2400
0200
0400
0600
0800
1000


NIGHT 1
BLC-LUT (n=8)
BLC-OC (n=8)
MELATONIN (PG/ML)
CLOCK TIME (HR)
0
5
10
15
20
25
30
35
40
45
50
2000
2200
2400
0200
0400
0600
0800
1000

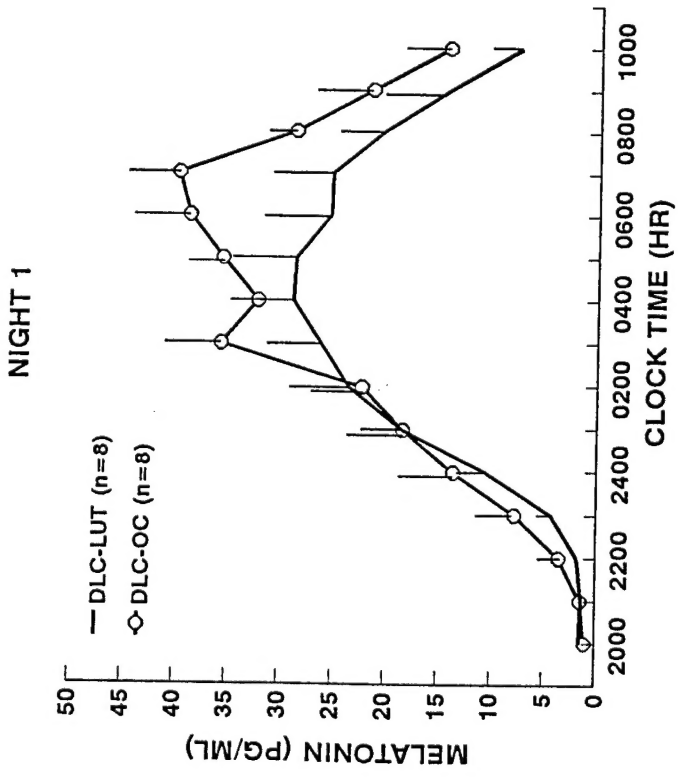
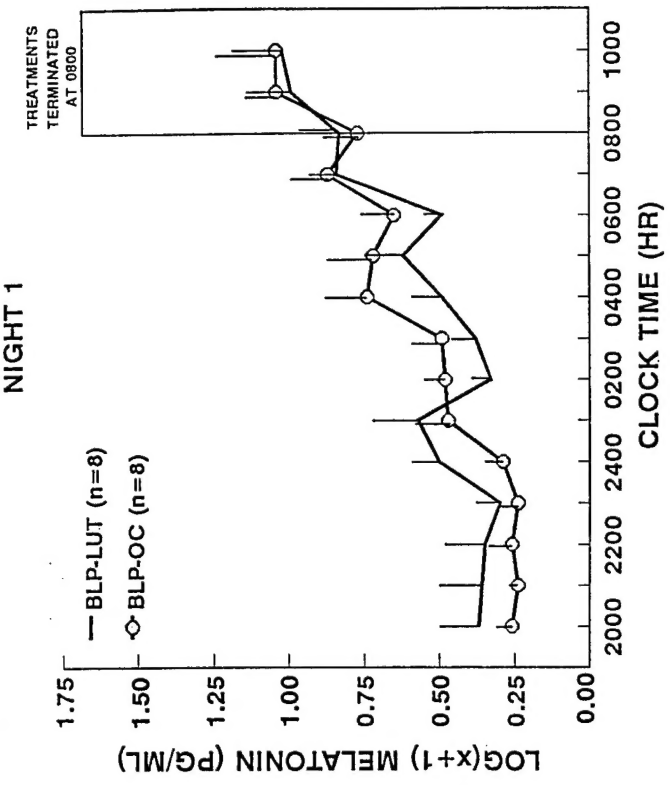
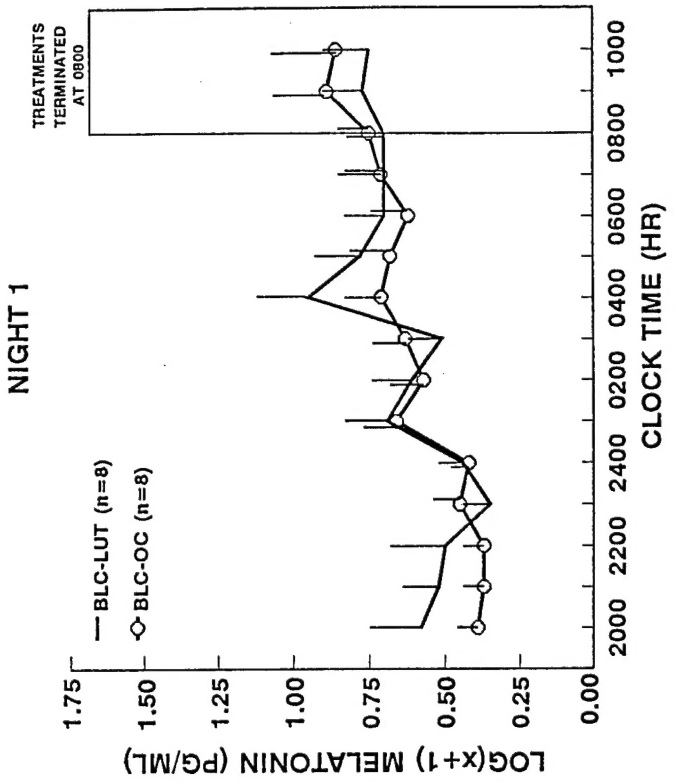
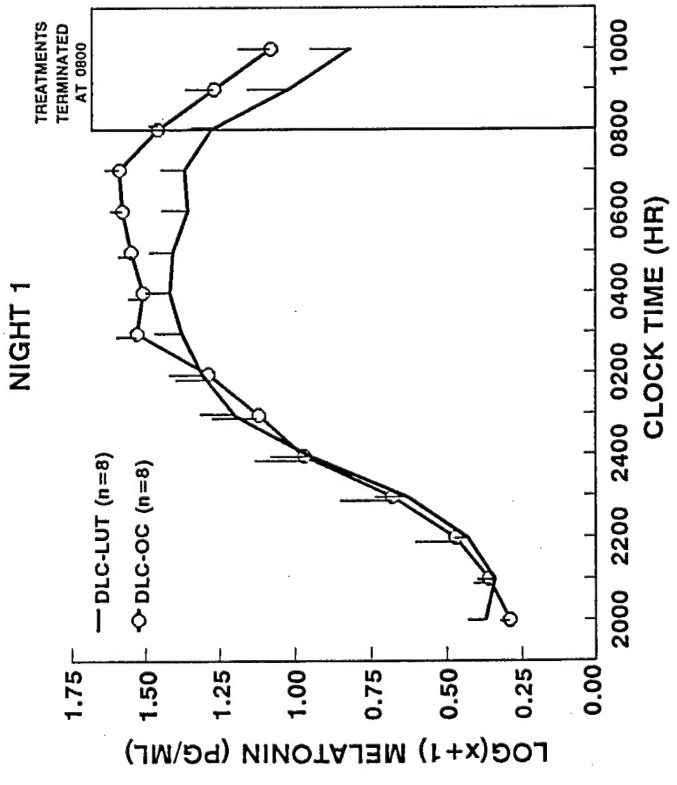
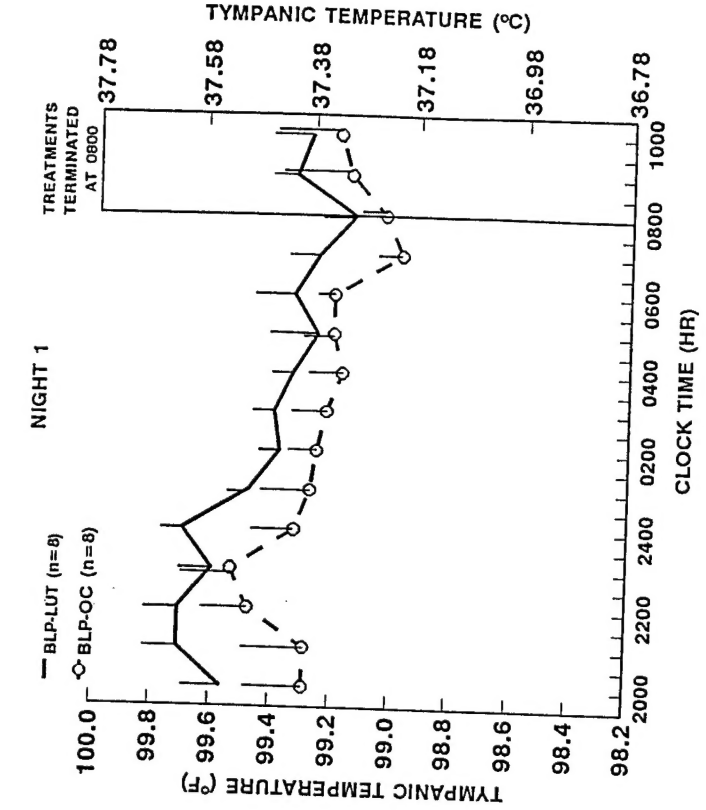

NIGHT 1
DLC-LUT (n=8)
DLC-OC (n=8)
MELATONIN (PG/ML)
CLOCK TIME (HR)
0
5
10
15
20
25
30
35
40
45
50
2000
2200
2400
0200
0400
0600
0800
1000

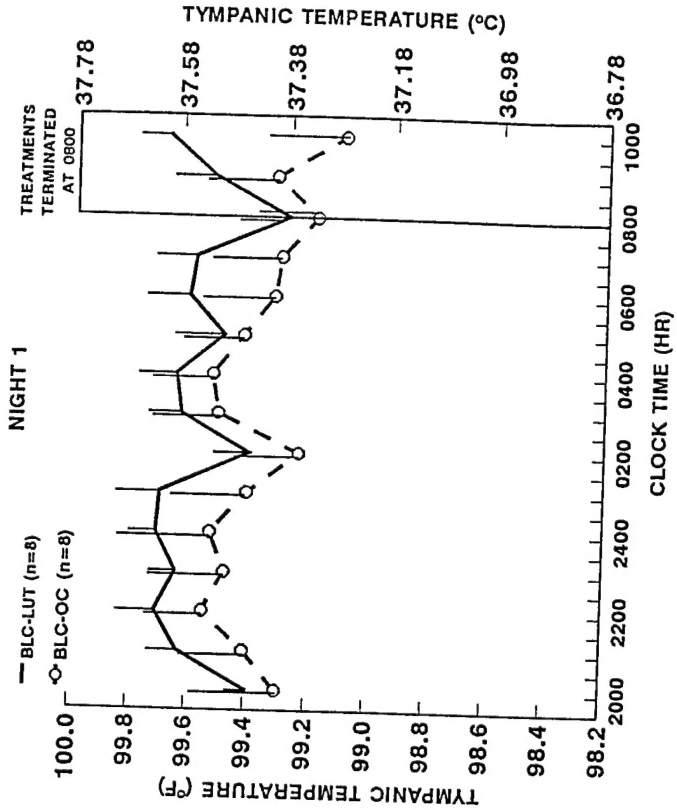
Figure 31


NIGHT 1
TREATMENTS TERMINATED AT 0800
BLP-LUT (n=8)
BLP-OC (n=8)
LOG(x+1) MELATONIN (PG/ML)
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
2000 2200 2400 0200 0400 0600 0800 1000
CLOCK TIME (HR)


NIGHT 1
TREATMENTS TERMINATED AT 0800
BLC-LUT (n=8)
BLC-OC (n=8)
LOG(x+1) MELATONIN (PG/ML)
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
2000 2200 2400 0200 0400 0600 0800 1000
CLOCK TIME (HR)


NIGHT 1
TREATMENTS TERMINATED AT 0800
DLC-LUT (n=8)
DLC-OC (n=8)
LOG(x+1) MELATONIN (PG/ML)
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
2000 2200 2400 0200 0400 0600 0800 1000
CLOCK TIME (HR)


TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
TREATMENTS TERMINATED AT 0800
NIGHT 1
BLP-LUT (n=8)
BLP-OC (n=8)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
TYMPANIC TEMPERATURE (°F)
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)


TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
TREATMENTS TERMINATED AT 0800
NIGHT 1
BLC-LUT (n=8)
BLC-OC (n=8)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
TYMPANIC TEMPERATURE (°F)
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

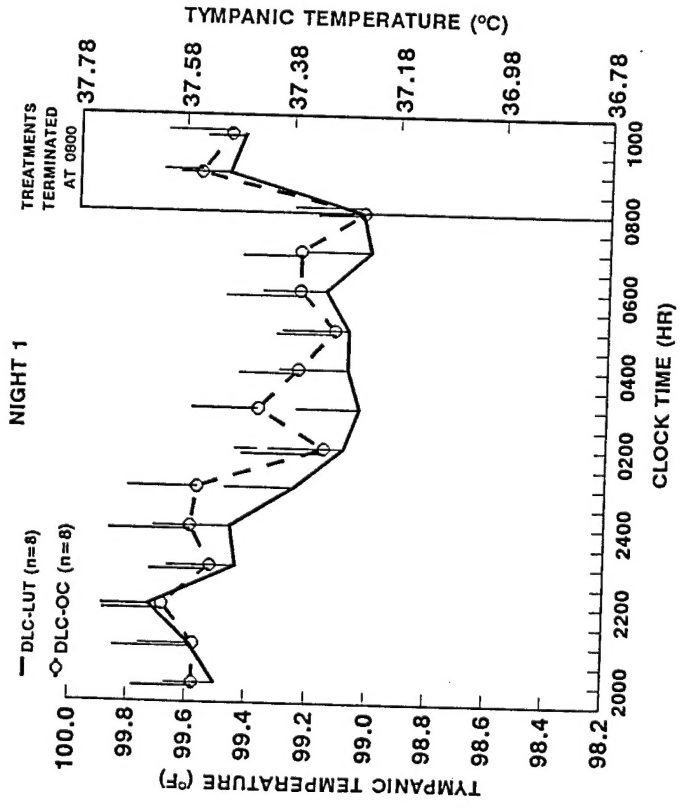
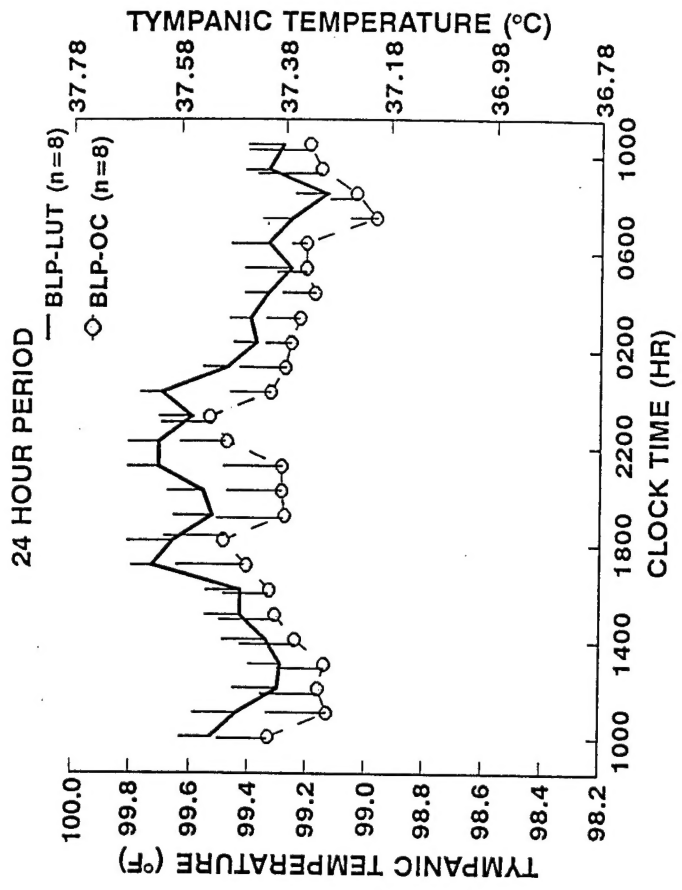
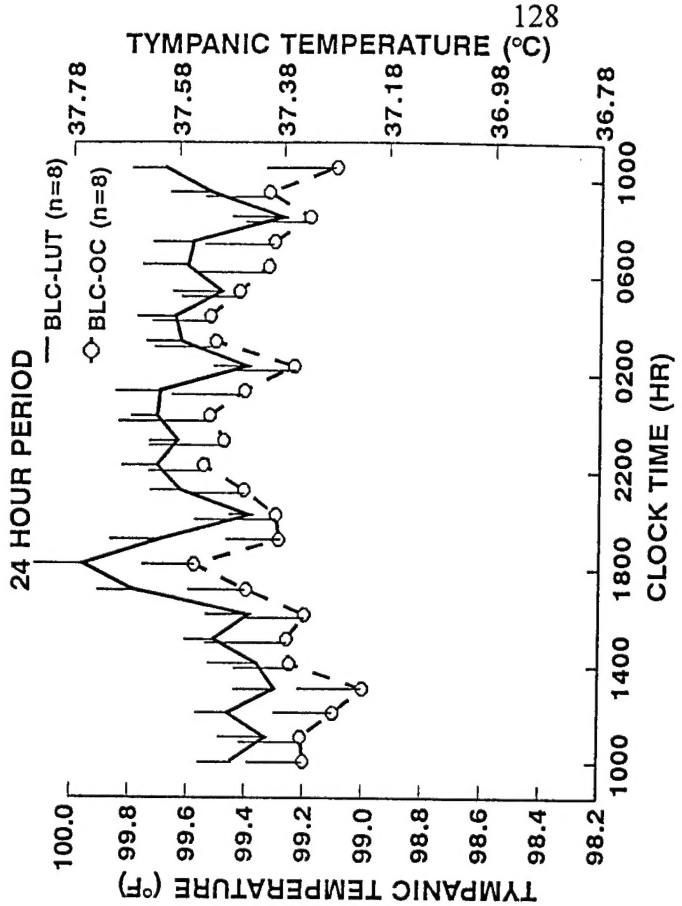

TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
TREATMENTS TERMINATED AT 0800
NIGHT 1
DLC-LUT (n=8)
DLC-OC (n=8)
100.0
99.8
99.6
99.4
99.2
99.0
98.8
98.6
98.4
98.2
TYMPANIC TEMPERATURE (°F)
2000
2200
2400
0200
0400
0600
0800
1000
CLOCK TIME (HR)

Figure 32


TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
BLP-LUT (n=8)
BLP-OC (n=8)
24 HOUR PERIOD
1000 1400 1800 2200 0200 0600 1000
CLOCK TIME (HR)
TYMPANIC TEMPERATURE (°F)
100.0 99.8 99.6 99.4 99.2 99.0 98.8 98.6 98.4 98.2


TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
BLC-LUT (n=8)
BLC-OC (n=8)
24 HOUR PERIOD
1000 1400 1800 2200 0200 0600 1000
CLOCK TIME (HR)
TYMPANIC TEMPERATURE (°F)
100.0 99.8 99.6 99.4 99.2 99.0 98.8 98.6 98.4 98.2

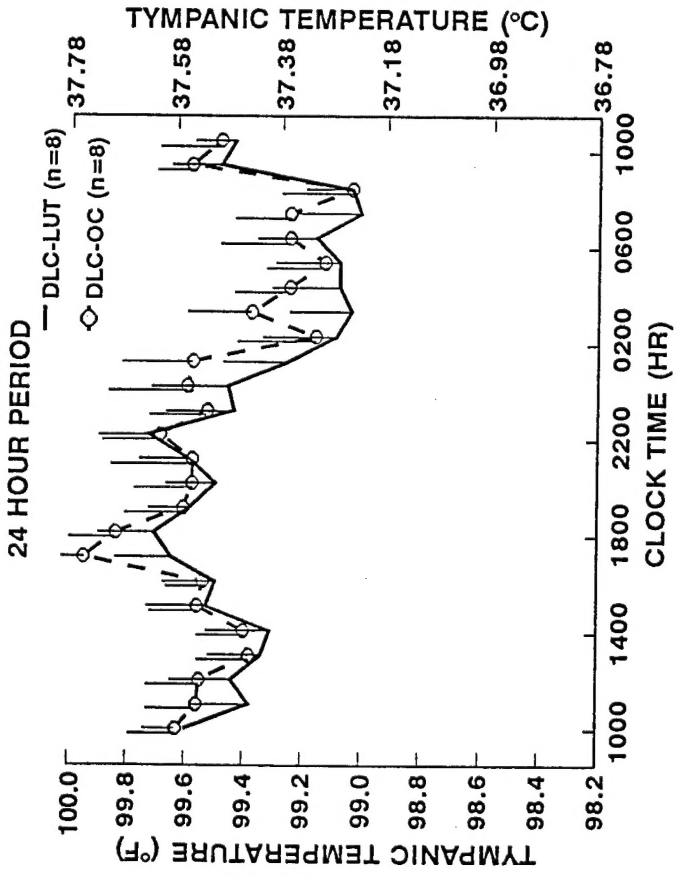

TYMPANIC TEMPERATURE (°C)
37.78
37.58
37.38
37.18
36.98
36.78
DLC-LUT (n=8)
DLC-OC (n=8)
24 HOUR PERIOD
1000 1400 1800 2200 0200 0600 1000
CLOCK TIME (HR)
TYMPANIC TEMPERATURE (°F)
100.0 99.8 99.6 99.4 99.2 99.0 98.8 98.6 98.4 98.2

Figure 33